Health Update:

Update 1: Swine Influenza

April 27, 2009

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Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

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912 Wildwood
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Health Update
April 27, 2009

IMPORTANT SWINE INFLUENZA INFORMATION – MUST BE SHARED WITH ALL MEDICAL STAFF

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 1: Swine Influenza**

This document provides updated information on swine influenza, including revised recommendations for submission of influenza specimens to the Missouri State Public Health Laboratory (MSPHL) from patients who meet specified criteria.

At the present time, 40 human cases of laboratory-confirmed swine influenza A (H1N1) virus infection have been identified in the United States. Seven cases have been reported from California, 2 cases from Kansas, 28 cases from New York City, 1 case from Ohio, and 2 cases from Texas. No cases have, to date, been reported from Missouri. As enhanced surveillance efforts continue, both in Missouri and nationally, it is anticipated that significantly more cases will be identified.

Human cases of swine influenza A (H1N1) virus infection have also been identified internationally, particularly in Mexico.

The Missouri Department of Health and Senior Services (DHSS) is conducting enhanced surveillance for possible swine influenza cases in humans. As part of this effort, MSPHL is performing polymerase chain reaction (PCR) testing for swine influenza virus on nasopharyngeal specimens from patients **who meet the following criteria**:

Person with a febrile influenza-like-illness (ILI)

WHO

a) Traveled to Mexico within 7 days preceding their illness

OR

b) Had contact with person with febrile illness who was in Mexico at some time during the 7 days preceding their illness

OR

c) Had contact within the past 7 days with a person who has confirmed swine influenza

OR

d) Lives in, or in the past 7 days has traveled to, the immediate area of a confirmed swine influenza case

Before any specimen is sent to MSPHL for testing, DHSS staff must first be consulted by calling 800-392-0272.

MSPHL can test specimens sent by any medical provider, including those in ambulatory settings, who has a patient that meets the above criteria. **Clinicians in hospital intensive care units and emergency departments are especially encouraged to send specimens from any of their patients meeting these criteria.** Initial test results should be available within 24 hours of the time the specimen is received by MSPHL.

DHSS continues to urge the existing network of Missouri influenza sentinel surveillance providers to submit specimens to MSPHL from outpatients who meet the definition for influenza-like illness, suspect or confirmed influenza, bacterial pneumonia, or febrile lower respiratory illness. For sentinel surveillance providers, consultation with DHSS prior to sending specimens is not required.

Because the virus is not currently believed to be highly pathogenic, specimen collection protocols are the same as for seasonal influenza. Clinicians should obtain a nasopharyngeal swab (using only the supplied Dacron / flocked swab or equivalent) for influenza testing and place it in a refrigerator (not a freezer), and then (following consultation with DHSS as described on the preceding page) send to MSPHL for testing. The Attachment to this Health Update contains detailed instructions for obtaining and submitting seasonal influenza specimens (as well as specimens from persons suspected of being infected with swine influenza virus).

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like-illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day - 7 days a week). All LPHAs are encouraged to perform enhanced, expedited investigations of any such clusters or outbreaks reported in their jurisdictions.

Current information on swine influenza from DHSS is available at: http://www.dhss.mo.gov/BT_Response/_SwineFlu09.html.

The Centers for Disease Control and Prevention (CDC) has issued a number of guidance documents related to swine influenza, including recommendations on infection control and the use of antiviral medications. These documents are available at http://www.cdc.gov/swineflu/guidance/.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Attachment

Missouri State Public Health Laboratory
COLLECTION AND SUBMISSION OF SEASONAL INFLUENZA SPECIMENS

Upon receipt of the virus shipping containers, place freeze pillows in freezer and keep frozen until specimens are packaged. Store TPB in a refrigerator (4-8ºC) until ready to use.

COLLECTION OF SPECIMEN

Swab: Use only the supplied Dacron / flocked swab or equivalent. Collect appropriate specimen for Influenza testing. Do not use wood shafted or cotton swabs for specimen collection. Break off swab tip into a vial of transport medium (TPB). Securely fasten the screw cap on the specimen tube. Keep the specimen cold (4-8ºC), pending shipment.

Tryptose Phosphate Broth (TPB) is the virus transport media to be used for Influenza testing and is supplied by the Department of Health. Commercially available viral (not bacterial) transport medium may also be used.

NOTE: After a swab is used, place it into the vial of transport medium and break off the swab tip low enough to allow the cap of the media tube to be tightly secured. If the swab is too long for the cap to fit tightly, the media will leak out and we will not be able to test the specimen. **MAKE SURE ALL SPECIMENS ARE LABELED WITH THE PATIENT'S NAME. ANY SPECIMENS RECEIVED WITHOUT PATIENT NAMES WILL BE DISCARDED WITHOUT TESTING.**

Temporary Storage of Specimens for Virus Culture

Specimens should be shipped to the State Laboratory as soon as possible. In order to ensure accuracy, relevance, and validity of testing and reports, specimens that are not received within 7 days of collection will not be tested unless the specimen has been kept at –70º C and shipped on dry ice. During temporary storage, remember that freezing and thawing can be detrimental to virus survival. It is best to keep specimens at refrigerator temperature during temporary storage. At warmer temperatures virus survival is diminished.

PACKING FOR SHIPMENT OF SPECIMENS FOR VIRUS CULTURE

Place refrigerant pillows in Styrofoam box. Pillows must be frozen when box is packed for shipment to maintain specimens at proper temperature. Place specimens in safety container provided in Styrofoam container with freezer pillows. Close lid on Styrofoam box and place completed form on top of Styrofoam box. Place Styrofoam box inside cardboard box and tape shut. **DO NOT USE ICE MADE WITH WATER WHEN SHIPPING SPECIMENS FOR TESTING.**

Shipment of Specimens for Virus Culture Testing

Determine method of shipment (mail or courier) that will get specimens to the Laboratory in the shortest length of time. If possible, select the method of shipment so that the specimens will not arrive in Jefferson City on Saturday, Sunday, or a holiday. **DO NOT SHIP CLINICAL SPECIMENS BY UPS**. **PLEASE USE THESE KITS FOR SEASONAL INFLUENZA SURVEILLANCE SPECIMENS ONLY.**

Missouri State Public Health Laboratory
101 North Chestnut Street, Jefferson City, MO 65101
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Revised: January 14, 2009

Health Update:

Update 2: Swine Influenza

April 28, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

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Health Update
April 28, 2009

IMPORTANT SWINE INFLUENZA INFORMATION – MUST BE SHARED WITH ALL MEDICAL STAFF

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 2: Swine Influenza**

This document provides updated information on swine influenza, including revised recommendations for submission of influenza specimens to the Missouri State Public Health Laboratory (MSPHL) from patients who meet specified criteria.

Current information on swine influenza from the Missouri Department of Health and Senior Services (DHSS) is available at: http://www.dhss.mo.gov/BT_Response/_SwineFlu09.html.

At the present time, 64 human cases of laboratory-confirmed swine influenza A (H1N1) virus infection have been identified in the United States. Ten cases have been reported from California, 2 cases from Kansas, 45 cases from New York City, 1 case from Ohio, and 6 cases from Texas. Five of those cases have been hospitalized; no deaths have been reported. Prompted by the growing outbreak, the World Health Organization (WHO) raised the Pandemic Alert Level to Phase 4, and the United States government declared a Public Health Emergency.

No cases have, to date, been reported from Missouri. As enhanced surveillance efforts continue, both in Missouri and nationally, it is anticipated that significantly more cases will be identified.

Human cases of swine influenza A (H1N1) virus infection continue to increase internationally, particularly in Mexico.

DHSS is conducting enhanced surveillance for possible swine influenza cases in humans. As part of this effort, MSPHL is performing polymerase chain reaction (PCR) testing for swine influenza virus on specimens from patients **who meet the following epidemiologic criteria**:

Person with a febrile influenza-like-illness (ILI)

WHO

a) Traveled to Mexico within 7 days preceding their illness

OR

b) Had contact with person with febrile illness who was in Mexico at some time during the 7 days preceding their illness

OR

c) Had contact within the past 7 days with a person who has confirmed swine influenza

OR

d) Lives in, or in the past 7 days has traveled to, the immediate area of a confirmed swine influenza case

Before any specimen is sent to MSPHL for testing, DHSS staff must first be consulted for sample submission by calling 800-392-0272.

If you are one of the DHSS-approved sentinel surveillance providers, consultation with DHSS prior to sending specimens is not required.

In order to enhance surveillance, clinicians in **hospital intensive care units and emergency departments should** submit specimens from any of their patients meeting the above-described epidemiologic criteria to MSPHL.

Other medical providers, including those in ambulatory or hospital settings, are encouraged to send specimens from suspect cases who meet the epidemiological criteria to MSPHL.

DHSS continues to urge the existing network of Missouri influenza sentinel surveillance providers to submit specimens to MSPHL from outpatients who meet the definition for influenza-like illness, suspect or confirmed influenza, bacterial pneumonia, or febrile lower respiratory illness.

Commercially available rapid influenza antigen tests have unknown sensitivity and specificity to detect human infection with swine influenza A (H1N1) virus in clinical specimens, and have suboptimal sensitivity to detect seasonal influenza viruses. Therefore, a negative rapid test could be a false negative, and should not be assumed a final diagnostic test for swine influenza infection.

Because the virus is not currently believed to be highly pathogenic, specimen collection protocols are the same as for seasonal influenza. The following should be collected as soon as possible after illness onset: nasopharyngeal swab/aspirate or nasal wash/aspirate. If these specimens cannot be collected, a combined nasal swab with an oropharyngeal swab is acceptable. For patients who are intubated, an endotracheal aspirate should also be collected.

If using a nasopharyngeal swab, use only the supplied Dacron / flocked swab or equivalent. Place it in a refrigerator (not a freezer), and then (following consultation with DHSS as described on the preceding page) send to MSPHL for testing. The Attachment to this Health Update contains detailed instructions for obtaining and submitting seasonal influenza specimens (as well as specimens from persons suspected of being infected with swine influenza virus).

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like-illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day - 7 days a week). All LPHAs are encouraged to perform enhanced, expedited investigations of any such clusters or outbreaks reported in their jurisdictions.

The Centers for Disease Control and Prevention (CDC) has issued a number of guidance documents related to swine influenza, including recommendations on infection control and the use of antiviral medications. These documents are available at http://www.cdc.gov/swineflu/guidance/.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Attachment

Missouri State Public Health Laboratory
COLLECTION AND SUBMISSION OF SEASONAL INFLUENZA SPECIMENS

Upon receipt of the virus shipping containers, place freeze pillows in freezer and keep frozen until specimens are packaged. Store TPB in a refrigerator (4-8ºC) until ready to use.

COLLECTION OF SPECIMEN

Swab: Use only the supplied Dacron / flocked swab or equivalent. Collect appropriate specimen for Influenza testing. Do not use wood shafted or cotton swabs for specimen collection. Break off swab tip into a vial of transport medium (TPB). Securely fasten the screw cap on the specimen tube. Keep the specimen cold (4-8ºC), pending shipment.

Tryptose Phosphate Broth (TPB) is the virus transport media to be used for Influenza testing and is supplied by the Department of Health. Commercially available viral (not bacterial) transport medium may also be used.

NOTE: After a swab is used, place it into the vial of transport medium and break off the swab tip low enough to allow the cap of the media tube to be tightly secured. If the swab is too long for the cap to fit tightly, the media will leak out and we will not be able to test the specimen. **MAKE SURE ALL SPECIMENS ARE LABELED WITH THE PATIENT'S NAME. ANY SPECIMENS RECEIVED WITHOUT PATIENT NAMES WILL BE DISCARDED WITHOUT TESTING.**

For interim guidance see: http://www.cdc.gov/swineflu/specimencollection.htm.

Temporary Storage of Specimens for Virus Culture

Specimens should be shipped to the State Laboratory as soon as possible. In order to ensure accuracy, relevance, and validity of testing and reports, specimens that are not received within 7 days of collection will not be tested unless the specimen has been kept at –70º C and shipped on dry ice. During temporary storage, remember that freezing and thawing can be detrimental to virus survival. It is best to keep specimens at refrigerator temperature during temporary storage. At warmer temperatures virus survival is diminished.

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Shipment of Specimens for Virus Culture Testing

Determine method of shipment (mail or courier) that will get specimens to the Laboratory in the shortest length of time. If possible, select the method of shipment so that the specimens will not arrive in Jefferson City on Saturday, Sunday, or a holiday. **DO NOT SHIP CLINICAL SPECIMENS BY UPS**. **PLEASE USE THESE KITS FOR SEASONAL INFLUENZA SURVEILLANCE SPECIMENS ONLY.**

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Phone# 573-751-3334
Fax # 573-526-2754

Revised: April 28, 2009

Health Update:

Update 3: Swine Influenza

April 29, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

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Health Update
April 29, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 3: Swine Influenza**

IMPORTANT SWINE INFLUENZA INFORMATION – MUST BE SHARED WITH ALL MEDICAL STAFF

This document provides updated information on swine influenza, including information on the availability of guidance documents for medical professionals on the management of different groups of persons with the disease.

Current information on swine influenza from the Missouri Department of Health and Senior Services (DHSS) is available at: http://www.dhss.mo.gov/BT_Response/_SwineFlu09.html.

At the present time, 90 human cases of laboratory-confirmed swine influenza A (H1N1) virus infection have been identified in the United States.

Arizona	1 case	Michigan	1 cases
California	14 cases	Nevada	1 case
Indiana	1 case	New York	51 cases
Kansas	2 cases	Ohio	1 case
Massachusetts	2 cases	Texas	16 cases

One fatality has been reported in a 22-month-old boy from Mexico City who died earlier this week in a hospital in the Houston, Texas area. According to the Texas Department of State Health Services, the boy, who had several underlying health problems, had traveled with his family to visit relatives in Texas. The boy developed a fever on April 8, followed by other influenza-like symptoms. He was admitted to a Brownsville, Texas hospital a few days later, and the next day was transferred to a Houston-area hospital where he died.

According to the Centers for Disease Control and Prevention (CDC), the more recent illnesses and the reported death suggest that a pattern of more severe illness associated with the swine influenza virus may be emerging in the U.S. Most people will not have immunity to this new virus and, as it continues to spread, more cases, more hospitalizations, and more deaths are expected in the coming days and weeks.

Young children and pregnant women are two groups of people who are at high risk of serious complications from seasonal influenza. CDC has issued new interim guidance for clinicians on how to care for children and pregnant women who may be infected with swine influenza virus.

Guidance for Clinicians on Prevention and Treatment in Young Children
http://www.cdc.gov/swineflu/childrentreatment.htm

Pregnant Women: Considerations for Clinicians
http://www.cdc.gov/swineflu/clinician_pregnant.htm

A more general guidance document from CDC on identifying and caring for patients with swine influenza was recently released. This document is available at http://www.cdc.gov/swineflu/identifyingpatients.htm.

In addition, CDC has issued a number of other guidance documents for medical providers related to swine influenza, including recommendations on infection control and the use of antiviral medications. These documents, which will be updated and expanded as the situation evolves, are available at http://www.cdc.gov/swineflu/guidance/.

DHSS is conducting enhanced surveillance for swine influenza in humans. As part of this effort, the Missouri State Public Health Laboratory (MSPHL) is performing polymerase chain reaction (PCR) testing for swine influenza virus on specimens from patients **who meet certain epidemiologic criteria**. See Health Update #2: Swine Influenza at http://www.dhss.mo.gov/BT_Response/HAds/HU2SwineFlu4-28-09.pdf for details, including submission criteria and acceptable specimens.

In order to enhance surveillance, clinicians in **hospital intensive care units and emergency departments should submit specimens from any of their patients meeting the epidemiologic criteria described in Health Update #2 to MSPHL**. Other medical providers, including those in ambulatory or hospital settings, are encouraged to send specimens from suspect cases who meet the epidemiological criteria to MSPHL.

Before any specimen is sent to MSPHL for testing, DHSS staff must first be consulted for sample submission by calling 800-392-0272.

For DHSS-approved sentinel surveillance providers, consultation with DHSS prior to sending specimens is not required.

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like-illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day - 7 days a week). All LPHAs are encouraged to perform enhanced, expedited investigations of any such clusters or outbreaks reported in their jurisdictions.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Health Update:

Update 4: Swine Influenza

May 1, 2009

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Health Update
May 1, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 4: Swine Influenza**

IMPORTANT SWINE INFLUENZA INFORMATION – MUST BE SHARED WITH ALL MEDICAL STAFF

The Centers for Disease Control and Prevention (CDC) today confirmed that a woman from Platte County, Missouri, was infected with swine influenza A (H1N1) virus. This is the state's first confirmed case. The patient, who is in her 30's, had recently traveled to Mexico. She received antiviral medication and was never admitted to a hospital. Health officials have informed all persons with whom she had direct contact so that they can receive appropriate medical care.

The Missouri Department of Health and Senior Services (DHSS) continues to conduct enhanced surveillance for swine influenza cases. As part of this effort, the Missouri State Public Health Laboratory (MSPHL) is performing polymerase chain reaction (PCR) testing for swine influenza virus on specimens from patients **who meet certain epidemiologic criteria**. See Health Update #2 - Swine Influenza for further details, including submission criteria and acceptable specimens. (This document is available on DHSS's website at http://www.dhss.mo.gov/BT_Response/HAds/HU2SwineFlu4-28-09.pdf) In addition to the submission criteria listed in Health Update #2, specimens will also now be accepted from patients with a febrile influenza-like illness who are admitted to a hospital. **Before any specimen is sent to MSPHL for testing, DHSS staff must first be consulted for sample submission by calling 800-392-0272.** For DHSS-approved sentinel surveillance providers, consultation with DHSS prior to sending specimens is not required.

SPECIAL SUNDAY LABORATORY COURIER PICK-UP May 3, 2009

In order to facilitate timely laboratory testing of approved specimens from persons suspected of being infected with swine influenza virus, MSPHL is implementing a Sunday courier pick-up at eight geographically-located hospitals across the state for May 3, 2009, for overnight delivery. This service is intended to provide a drop site for DHSS-approved (see preceding paragraph) clinical specimens that are to be sent to MSPHL for analysis. **Only properly packaged specimens will be accepted.** The hospital site will not be responsible for packaging the specimens and therefore reserves the right to refuse a specimen for delivery. All specimens must arrive at the designated hospital location prior to 12:00 p.m. on May 3, 2009, for this service to be utilized. The eight hospitals that have agreed to partner with MSPHL to provide this service are listed on the following page.

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day - 7 days a week).

Information and links to clinical guidance documents for Missouri medical providers are available on the DHSS Swine Influenza website, at: http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

FACILITY	COUNTY	DESIGNATED LOCATION
N.E. Regional Medical Center 315 South Osteopathy Drive Kirksville	Adair County	1st Floor Lab
Columbia Regional Hospital 404 Keene Street Columbia	Boone County	1st Floor, Room 1177
Phelps Co. Reg. Med. Center 1000 West 10th Street Rolla	Phelps County	Front Office Lab
Children's Hospital 1 Children's Place St. Louis	St. Louis County	Room 2 North 25
St. John's Reg. Med. Center 2727 McClelland Blvd Joplin	Jasper County	Lab, 1st Floor
St. Francis Medical Center 211 St. Francis Drive Cape Girardeau	Cape Girardeau County	1st Floor Lab
St. John's Reg. Med. Center 1235 East Cherokee Springfield	Greene County	Lab, 2nd Floor
St. Luke's Hospital KC 4401 Wornall Road Kansas City	Jackson County	Reference Laboratory

Health Update:

Update 5: Swine Influenza

May 8, 2009

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Health Update
May 8, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 5: Swine Influenza**

IMPORTANT SWINE INFLUENZA INFORMATION – MUST BE SHARED WITH ALL MEDICAL STAFF

At the present time, 10 confirmed and 4 probable cases of swine influenza (H1N1) infection have been reported in Missouri. This number is expected to increase as additional clinical specimens are tested. (The most recently updated case count can be seen by going to the Missouri Department of Health and Senior Services [DHSS] Swine Flu website at http://www.dhss.mo.gov/BT_Response/_H1N1Flu.html.)

Public health officials are continuing to investigate this disease. According to the Centers for Disease Control and Prevention (CDC), "many patients who have had novel influenza (H1N1) virus infection, but who are not in a high-risk group have had a self-limited respiratory illness similar to typical seasonal influenza." CDC also indicates that treatment efforts should be directed primarily at persons who are hospitalized or at higher risk for influenza complications. Additional information, including recently updated (May 6) treatment recommendations, is available in a CDC guidance document at: http://www.cdc.gov/h1n1flu/recommendations.htm.

CDC has issued a number of other guidance documents on swine influenza (H1N1) for medical providers and public health officials. All of these document, which are being continually updated, are available at http://www.cdc.gov/h1n1flu/guidance/.

Important Change in DHSS Criteria for Accepting Specimens for Testing at the Missouri State Public Health Laboratory (MSPHL)

DHSS has been conducting surveillance for swine influenza (H1N1) cases. As part of this effort, MSPHL has been performing polymerase chain reaction (PCR) testing on specimens from patients with suspected swine influenza (H1N1) virus infection who have met specific criteria described in past Health Updates. Because the epidemiology and characteristics of swine influenza (H1N1) have now become better understood (and appear to generally be similar to those of seasonal influenza), there is no longer the need for the more intense case finding that has been in place for the past two weeks. For this reason, and in order to make the best use of available laboratory resources, **DHSS has changed the criteria that it will use in making decisions on which specimens to accept for testing at MSPHL**. **At the present time, the following are the only specimens that will be tested:**

1. **Persons with an acute febrile respiratory illness who are, or will immediately be, hospitalized.** (Acute febrile respiratory illness is defined as a measured temperature $\geq 100^0$ F and recent onset of at least one of the following: rhinorrhea or nasal congestion, sore throat, or cough.)
2. **Persons who are part of an outbreak investigation being conducted by DHSS and/or local public health agency (LPHA) staff.**

Before any specimen is sent to MSPHL for testing, DHSS staff must first be consulted for sample submission by calling 800-392-0272. For DHSS-approved sentinel surveillance providers, consultation with DHSS prior to sending specimens is not required.

SPECIAL SUNDAY LABORATORY COURIER PICK-UP
May 10, 2009

In order to facilitate timely laboratory testing of approved specimens from persons suspected of being infected with swine influenza virus, MSPHL is implementing a Sunday courier pick-up at eight geographically-located hospitals across the state for May 10, 2009, for overnight delivery. This service is intended to provide a drop site for DHSS-approved (see preceding section) clinical specimens that are to be sent to MSPHL for analysis. **Only properly packaged specimens will be accepted.** The hospital site will not be responsible for packaging the specimens and therefore reserves the right to refuse a specimen for delivery. All specimens must arrive at the designated hospital location prior to 12:00 p.m. on May 10, 2009, for this service to be utilized. The eight hospitals that have agreed to partner with MSPHL to provide this service are listed below.

FACILITY	COUNTY	DESIGNATED LOCATION
N.E. Regional Medical Center 315 South Osteopathy Drive Kirksville	Adair County	1st Floor Lab
Columbia Regional Hospital 404 Keene Street Columbia	Boone County	1st Floor, Room 1177
Phelps Co. Reg. Med. Center 1000 West 10th Street Rolla	Phelps County	Front Office Lab
Children's Hospital 1 Children's Place St. Louis	St. Louis County	Room 2 North 25
St. John's Reg. Med. Center 2727 McClelland Blvd Joplin	Jasper County	Lab, 1st Floor
St. Francis Medical Center 211 St. Francis Drive Cape Girardeau	Cape Girardeau County	1st Floor Lab
St. John's Reg. Med. Center 1235 East Cherokee Springfield	Greene County	Lab, 2nd Floor
St. Luke's Hospital KC 4401 Wornall Road Kansas City	Jackson County	Reference Laboratory

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day - 7 days a week).

More information for Missouri medical providers is available on the DHSS Swine Influenza website, at: http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Health Update:

Update 6:
Important Changes Related to Novel Influenza A H1N1 Testing Performed By the Missouri State Public Health Laboratory

June 9, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Update
June 9, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update 6: Important Changes Related to Novel Influenza A H1N1 Testing Performed By the Missouri State Public Health Laboratory**

Over the past couple of months the Missouri State Public Health Laboratory (MSPHL) has been conducting surveillance for the Novel Influenza A (H1N1) virus by performing polymerase chain reaction (PCR) testing on patients with influenza-like illness (ILI) to develop a better understanding of the epidemiology of this disease. As more has been learned, the testing strategies have changed from a broader to a more focused testing structure. The testing protocols that have been employed have been based on direction from the Centers for Disease Control and Prevention (CDC) as well as local and state information. In the previous Health Update, testing had been reduced to performing tests only on persons hospitalized with an ILI. This would allow the CDC and state health departments to have a better understanding of the epidemiology of Novel Influenza A (H1N1) infection. This Health Update is to inform you that the Missouri Department of Health and Senior Services (DHSS), in collaboration with the CDC, has decided to stop requesting information on individual Novel Influenza A (H1N1) cases, including those in special groups, such as pregnant women, health care workers, or hospitalized persons. With this information, along with the fact that approximately 77 percent of all isolates (CDC data) of influenza A are currently Novel Influenza A (H1N1), DHSS will return to a testing protocol that is consistent with seasonal influenza practices and will no longer be accepting routine specimens for Novel H1N1 testing.

Novel H1N1 PCR testing will be performed only under the following circumstances:

1. The SPHL will *only test* sentinel provider specimens; and
2. Those specimens submitted for epidemiological investigation purposes (e.g., as identification of a respiratory disease that hasn't been diagnosed and is part of an outbreak being investigated by the state or local health departments).

The Sentinel Providers will be returning to traditional testing for the off-season. The expectation is for us to receive a total of 3 specimens from each provider for the period June – October 1, 2009 and for the sentinel providers to submit their weekly office data to the national sentinel provider data base.

In situations other than those listed in 1 and 2, health care providers who wish individual patient testing can do so through commercial laboratories.

The MSPHL will routinely batch and test influenza specimens every Thursday except in outbreak situations.

All medical providers should immediately report any observed clusters or outbreaks of febrile influenza-like illness to the local public health agency (LPHA), or to DHSS at 800-392-0272 (24 hours a day – 7 days a week).

More information for Missouri medical providers is available on the DHSS Swine Influenza website, at: http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Questions should be directed to the LPHA, or to DHSS's Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Health Update:

Update: Febrile Reactions Following Gastrointestinal Endoscopy Procedures

July 14, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Update
July 14, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update: Febrile Reactions Following Gastrointestinal Endoscopy Procedures**

This is an update to the July 2 Health Advisory "Febrile Reactions Following Gastrointestinal Endoscopy Procedures", which reported the recent occurrence of cases of non-respiratory febrile reactions following gastrointestinal endoscopy procedures. Symptoms, which occurred a few hours after the procedures, were chills, aches, and fever up to 103.5^0F, with fairly quick resolution.

Subsequent investigation by the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and other public health agencies (including the St. Louis County Department of Health) has revealed that all affected patients received the anesthetic propofol from 100 mL vials manufactured by Teva Pharmaceutical Industries. Testing conducted by FDA revealed that two lots of this product used in facilities reporting reactions were positive for elevated levels of endotoxin. The lots are 31305429B and 31305430B. Teva Pharmaceuticals is initiating a voluntary recall for these lots, and clinicians are advised to immediately stop using these lots of Teva Pharmaceuticals propofol. CDC, FDA, and Teva Pharmaceutical Industries are continuing to investigate this issue.

The Missouri Department of Health and Senior Services (DHSS) continues to ask medical providers to report any cases of febrile reactions following gastrointestinal endoscopy procedures to DHSS at 800/392-0272 (24/7).

Questions should be directed to DHSS' Bureau of Communicable Disease Control and Prevention at 573/864-5317, or 800/392-0272.

Missouri Department of Health & Senior Services

Health Update:

Novel H1N1 Influenza Update 7: Current Situation, Clinical Issues, Testing Policies, and Planning/Response Actions for Outpatient Medical Facilities

July 28, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Update
July 28, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Novel H1N1 Influenza Update 7: Current Situation, Clinical Issues, Testing Policies, and Planning/Response Actions for Outpatient Medical Facilities**

This Health Update on novel H1N1 influenza summarizes the present situation in Missouri, discusses selected clinical issues, and describes the current testing policies of the Missouri State Public Health Laboratory. In addition, it lists 10 critical planning and response actions that medical offices and outpatient facilities should be taking to prepare for the potentially very large numbers of novel H1N1 influenza cases that may be seen in the coming months.

Current Situation in Missouri

In the Northern Hemisphere, novel influenza A (H1N1) virus is persisting, and is continuing to cause outbreaks and sporadic cases in numerous locales despite the onset of summer. In Missouri, 80 confirmed cases of novel H1N1 influenza, including one death, have been reported as of July 23, 2009. (See http://www.dhss.mo.gov/BT_Response/_H1N1Flu.html for more details.) Because specific testing for novel H1N1 influenza virus infection has been limited, the actual number of persons in Missouri who have been infected with the virus is undoubtedly much higher. Outbreaks of influenza-like illness (ILI) have occurred in recent weeks in youth camps in the state; individuals involved in six of these outbreaks have tested positive for novel H1N1 influenza virus. It appears likely that infections with this virus are occurring throughout the state, although their exact number cannot be estimated. Currently, the overall level of influenza activity in Missouri is reported as sporadic.

Selected Clinical Issues

Guidance for clinicians in managing patients with novel H1N1 influenza virus infection is available at http://www.cdc.gov/h1n1flu/clinicians/.

The Centers for Disease Control and Prevention (CDC) is currently recommending antiviral treatment for two groups of persons:

1. All hospitalized patients with confirmed, probable, or suspected novel H1N1 influenza.
2. Patients with confirmed, probable, or suspected novel H1N1 influenza who are at higher risk for seasonal influenza complications. (For a listing of groups at higher risk, see http://www.cdc.gov/h1n1flu/identifyingpatients.htm#groupsatrisk.)

CDC also recommends that if a patient is not in a high-risk group or is not hospitalized, then healthcare providers should use clinical judgment to guide treatment decisions. Many patients who have had novel H1N1 influenza virus infection, but who are not in a high-risk group have had a self-limited respiratory illness similar to typical seasonal influenza. For most of these patients, the benefits of using antivirals may be modest.

Guidance for antiviral use is found at http://www.cdc.gov/h1n1flu/recommendations.htm.

The Missouri Department of Health and Senior Services (DHSS) has a Web site for medical professionals which provides links to comprehensive information on novel H1N1 influenza. This site is located at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

CDC has stated that infection with novel H1N1 influenza virus appears to result in a spectrum of illness similar to that caused by seasonal influenza viruses. While many infections with novel H1N1 influenza virus are relatively mild, some persons have had severe or even fatal infections. Included here are individuals who developed rapidly

progressive lower respiratory tract disease resulting in respiratory failure, development of acute respiratory distress syndrome (ARDS), and prolonged intensive care unit (ICU) admission.

Thus far, most cases of illness, hospitalization, and death associated with novel H1N1 influenza virus infection have occurred among persons less than 65 years of age. Groups at increased risk of influenza-related complications include pregnant women, those with asthma, COPD, diabetes, chronic cardiovascular disease, and immunocompromised persons. These are the same groups as previously recognized to increase the risk of severe illness from seasonal influenza. In addition, morbid obesity may represent an additional risk factor for severe illness (see below). It should also be noted, however, that fatal disease associated with novel H1N1 influenza has occurred among persons without these conditions who previously were healthy.

Widespread susceptibility to this virus among young persons and the potential for large numbers of cases raises the possibility of more hospitalizations and deaths especially among younger age groups than would be expected for a typical routine seasonal influenza virus.

Evidence from previous pandemics and from seasonal influenza suggests that pregnant women are likely to be at increased risk of morbidity and mortality related to infection with novel H1N1 influenza virus. The impact of this virus on the newborn is unknown, but based on previous experience, newborns are expected to be at increased risk of severe illness.

Guidance for managing specific patient populations (e.g., pregnant women, young children) is available from CDC at http://www.cdc.gov/h1n1flu/clinicians/#specific.

Neurologic complications have been described previously in association with respiratory tract infection with seasonal influenza A or B viruses, and a recent CDC report described four children with neurologic complications associated with novel H1N1 influenza virus infection who had been admitted to hospitals in Dallas County, Texas. Patients were aged 7-17 years and were admitted with signs of ILI and seizures or altered mental status. All four patients recovered fully and had no neurologic sequelae at discharge. CDC states that these findings indicate that, as with seasonal influenza, neurologic complications can occur after respiratory tract infection with novel H1N1 influenza virus. CDC recommends that for children who have ILI accompanied by unexplained seizures or mental status changes, clinicians should consider acute seasonal influenza or novel H1N1 influenza virus infection in the differential diagnosis, send respiratory specimens for appropriate diagnostic testing, and promptly initiate empirical antiviral treatment, especially in hospitalized patients. Clinicians should not wait for the results of diagnostic testing before beginning treatment. Additional cases of children with neurologic complications are likely to be reported as the pandemic continues, and clinicians should remain aware of the potential for severe neurologic sequelae associated with seasonal or novel H1N1 influenza virus infection. [*MMWR* 2009; 58(28);773-8. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5828a2.htm) This report contains additional information on the clinical course and management of these patients, as well as clinical care recommendations for patients with ILI and neurologic signs/symptoms.]

The possible relationship between obesity and severe disease in persons with novel H1N1 influenza virus infection is currently being evaluated. A CDC report has summarized the clinical characteristics of a small series of 10 patients with novel H1N1 influenza virus infection and ARDS at a tertiary-care ICU in Michigan. Of the 10 patients, nine were obese (body mass index [BMI] ≥30), including seven who were extremely obese (BMI ≥40); five had pulmonary emboli; and nine had multiorgan dysfunction syndrome (MODS). Three patients died. It is not presently known whether obesity is an independent risk factor for severe complications of novel H1N1 influenza virus infection. However, CDC recommends that clinicians be aware of the potential for severe complications of infection with this virus, particularly in extremely obese patients. [*MMWR* 2009; 58(27):749-52. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5827a4.htm) Contained in this report is further information on the clinical course and management of these patients, as well as recommendations for clinicians caring for patients with novel H1N1 influenza virus infection.]

Higher oseltamivir dosing and longer duration of treatment have been suggested for H5N1 (avian influenza) patients with severe pulmonary disease. CDC has stated that until additional data are available, higher oseltamivir dosage (e.g., 150 mg orally twice a day for adults) or extending the duration of treatment can be

considered for severely ill hospitalized patients with novel H1N1 influenza virus infection. [*MMWR* 2009; 58(27):749-52. (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5827a4.htm)]

Vaccines for novel H1N1 influenza virus are presently under development. Current information is available from CDC at http://www.cdc.gov/h1n1flu/vaccination/public/vaccination_qa_pub.htm.

Laboratory Testing

The Missouri State Public Health Laboratory (MSPHL) is currently following a testing protocol that is consistent with seasonal influenza practices and is not accepting routine specimens for novel H1N1 influenza virus testing. MSPHL will only be performing testing for this virus under the following circumstances:

1. Specimens submitted by Influenza Sentinel Providers, or
2. Specimens submitted for epidemiological investigation purposes (i.e., as part of an outbreak being investigated by DHSS, local public health agencies, and/or CDC).

[Note for Influenza Sentinel Providers: Sentinel Providers have returned to their traditional off-season testing protocol. DHSS requests that a minimum of 3 specimens be sent from each Sentinel Provider during the period from June 1 through September 30. Sentinel Providers should also submit their weekly office data to the Influenza Sentinel Physicians Surveillance Network Database.]

Planning and Response Actions for Medical Offices and Outpatient Facilities

It is anticipated that when the regular influenza season begins later this year, the potential will exist for very large numbers of infections caused by novel H1N1 influenza virus to occur, especially given evidence that population immunity to this virus is low, particularly among the young. There is additional concern that during the summer the virus might undergo mutations that would cause it to become more transmissible or more virulent. Whether this will actually occur is not known, but is being monitored closely by public health officials worldwide.

Now is the time for all medical facilities to plan and, as appropriate, begin to implement actions to allow them to continue operation during an influenza pandemic. CDC has recently released a document entitled ***10 Steps You Can Take: Actions for Novel H1N1 Influenza Planning and Response for Medical Offices and Outpatient Facilities*** to assist these facilities in this process. This document is reproduced below, beginning on the next page.

As new information becomes available, DHSS will issue additional Health Updates.

Questions on novel H1N1 influenza should be directed to your local public health agency, or to DHSS' Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

10 Steps You Can Take: Actions for Novel H1N1 Influenza Planning and Response for Medical Offices and Outpatient Facilities

Centers for Disease Control and Prevention (CDC)

July 14, 2009

http://www.cdc.gov/h1n1flu/10steps.htm

It is critical to assure that medical offices and other outpatient facilities (e.g., outpatient/ambulatory clinics, outpatient surgery centers, urgent care centers, physical therapy/rehabilitation offices or clinics) that provide routine, episodic, and/or chronic healthcare services can manage an increased demand for services in the midst of a novel H1N1 influenza outbreak. Ensuring a sustainable community healthcare response will be important for a likely recurrence of novel H1N1 flu in the fall. See CDC's H1N1 Web site at http://www.cdc.gov/h1n1flu/ for up-to-date information.

1. Develop a Business Continuity Plan – Novel H1N1 flu outbreaks will impact your organization, employees, suppliers of critical materiel, and your family. Identify your office/clinic's essential functions and the individuals who perform them. Make sure you have trained enough people to properly work in these essential functions and allow for potential absenteeism. Develop a plan that will sustain your core business activities for several weeks. Make sure you have alternate plans for critical supplies in case there is disruption in your supply chains. For information about planning see: http://www.ready.gov/business/plan/index.html.

2. Inform employees about your plan for coping with additional surge during pandemic – Provide clear and frequent communication to ensure that your staff are aware and understand the plan. Explain any policies and procedures that will be used to protect staff and your patients, and to manage a surge of patients. Improve the resiliency of your staff by advising that employees have a pandemic family plan or personal plans.

3. Plan to operate your facility if there is significant staff absenteeism – Are you ready for 20 to 40% of your employees not being able to come to work? Cross training your staff is key to resilience here. What else can be done to assure continuity of operations with reduced staff?

4. Protect your workplace by asking sick employees to stay home – Be sure to ask sick staff to stay home. All personnel should self monitor daily for signs and symptoms of febrile respiratory illness. Staff who develop these symptoms should be instructed not to report to work, or if at work, should cease patient care activities and notify their supervisor. Be sure to align your sick leave policies so ill staff can stay home. See *What to Do If You Get Flu-Like Symptoms* at http://www.cdc.gov/h1n1flu/sick.htm for more information.

5. Plan for a surge of patients and increased demands for your services –Consider using your telephone system to deliver messages to incoming callers about when to seek medical care at your facility, when to seek emergency care, and where to go for information about caring for a person with flu at home (see *Taking Care of a Sick Person in Your Home* at http://www.cdc.gov/h1n1flu/guidance_homecare.htm). Consider extending your hours of operation to include telephone triage of patients during a community outbreak.

6. Care for patients with novel H1N1 flu in your facility – Make plans to screen patients for signs and symptoms of febrile respiratory illness at entry to the facility. If feasible, use separate waiting and exam rooms for possible novel H1N1 flu patients; plan to offer surgical masks to symptomatic patients who are able to wear them (adult and pediatric sizes should be available), provide facial tissues, receptacles for their disposal, and provide hand hygiene products in waiting areas and examination rooms. For information on caring for patients see: *Interim Guidance for Clinicians on Identifying and Caring for Patients with Swine-origin Influenza A (H1N1) Virus Infection* at http://www.cdc.gov/h1n1flu/identifyingpatients.htm.

7. Take steps to protect the health of your workforce during an outbreak of H1N1 – All healthcare personnel who come in close contact with patients who may have novel H1N1 flu should take precautions to include use of respiratory and eye protection for all patient care activities (see: *Healthcare Workplaces Classified as Very High or High Exposure Risk for Pandemic Influenza* at http://www.osha.gov/Publications/exposure-risk-classification-factsheet.html). For information on the use of infection control measures including use of personal protective equipment for staff, see *Interim Guidance for Infection Control for Care of Patients with Confirmed or Suspected Novel H1N1 influenza virus Infection in a*

Healthcare Setting at http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm. Plan now to stockpile sufficient PPE for your staff. (see: *Proposed Guidance on Workplace Stockpiling of Respirators and Facemasks for Pandemic Influenza* at http://www.osha.gov/dsg/guidance/stockpiling-facemasks-respirators.html).

8. Provide immunization against seasonal flu at no cost to your staff – In the fall there may be several influenza strains circulating at the same time. Although seasonal flu immunization will not provide protection to novel H1N1 influenza, annual influenza vaccination is recommended for health care professionals and will likely protect against seasonal influenza strains. See: *Influenza Vaccination of Health-Care Personnel* at http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5502a1.htm?s_cid=rr5502a1_e.

9. Make sure you know about the pandemic planning and response activities of the hospitals, outpatient facilities and local public health in your community – Actively seek information from and coordinate with key medical, clinical facilities and public health departments in your community to learn about how they will manage patients during a pandemic. Medical offices, emergency rooms, urgent care centers and hospitals in communities with outbreaks will likely have difficulty managing a large influx of patients; a coordinated community response is important to manage surge and assure optimal patient care. Develop a plan to manage your patients who do not need to seek emergency services.

10. Plan now so you will know where to turn to for reliable, up-to-date information in your local community – Staff in healthcare settings should monitor the CDC H1N1 Flu Web site and local/State health department Web sites for the latest information. For local health department contact information, see http://www.naccho.org/about/lhd/. [The Missouri Department of Health and Senior Services (DHSS) Web site address is http://www.dhss.mo.gov/, and the address for DHSS' H1N1 Flu Web site is http://www.dhss.mo.gov/BT_Response/_H1N1Flu.html.]

Be prepared for a range of situations. The true impact of novel H1N1 flu outbreaks in the coming months will not be known until it happens. Be prepared for a possibility that your facility will have significant increased demand for services and the possibility that the fall outbreak may have greater impact than the outbreak in the spring, 2009.

For more information see the *Medical Offices and Clinics Pandemic Influenza Planning Checklist* at http://pandemicflu.gov/plan/healthcare/medical.html. Also sign up to receive regular updates about novel H1N1 influenza, emerging infectious diseases, and other emergency preparedness and response information by going to www.emergency.cdc.gov/clinregistry.

Missouri Department of Health & Senior Services

Health Update:

Novel H1N1 Influenza Update 8: Worldwide Illness Patterns, Serious Disease Risk in Pregnant Women, Rapid Influenza Tests, New Guidance for Ill Persons, Vaccine Issues

August 10, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Update
August 10, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Novel H1N1 Influenza Update 8: Worldwide Illness Patterns, Serious Disease Risk in Pregnant Women, Rapid Influenza Tests, New Guidance for Ill Persons, Vaccine Issues**

This Health Update contains the following:

- A recent summary of worldwide patterns of illness associated with novel influenza A (H1N1) virus infection.
- A report on increased risk of serious disease in pregnant women infected with novel H1N1 virus, and current recommendations on their management.
- Guidance on proper interpretation of rapid influenza diagnostic tests.
- New recommendations for persons with influenza-like illness.
- Links to information on development and anticipated use of a vaccine for novel H1N1 virus.

Worldwide Illnesses Patterns Associated With Novel H1N1 Virus Infection

On July 31, the World Health Organization (WHO) provided the following updated information on illness patterns associated with novel H1N1 virus infection:

> Worldwide, the majority of patients infected with the pandemic virus continue to experience mild symptoms and recover fully within a week, even in the absence of any medical treatment. Monitoring of viruses from multiple outbreaks has detected no evidence of change in the ability of the virus to spread or to cause severe illness.
>
> In addition to the enhanced risk documented in pregnant women, groups at increased risk of severe or fatal illness include people with underlying medical conditions, most notably chronic lung disease (including asthma), cardiovascular disease, diabetes, and immunosuppression. Some preliminary studies suggest that obesity, and especially extreme obesity, may be a risk factor for more severe disease.
>
> Within this largely reassuring picture, a small number of otherwise healthy people, usually under the age of 50 years, experience very rapid progression to severe and often fatal illness, characterized by severe pneumonia that destroys the lung tissue, and the failure of multiple organs. No factors that can predict this pattern of severe disease have yet been identified, though studies are under way.
>
> Clinicians, patients, and those providing home-based care need to be alert to danger signs that can signal progression to more severe disease. As progression can be very rapid, medical attention should be sought when any of the following danger signs appear in a person with confirmed or suspected H1N1 infection:
>
> - shortness of breath, either during physical activity or while resting
> - difficulty in breathing
> - turning blue
> - bloody or colored sputum
> - chest pain
> - altered mental status
> - high fever that persists beyond 3 days
> - low blood pressure
>
> In children, danger signs include fast or difficult breathing, lack of alertness, difficulty in waking up, and little or no desire to play.
> (http://www.who.int/csr/disease/swineflu/notes/h1n1_pregnancy_20090731/en/index.html)

A brief summary of the current situation in Missouri was provided in the preceding (July 28) Health Update, available at http://www.dhss.mo.gov/BT_Response/HAds/HU7SwineFlu7-28-09.pdf.

Pregnant Women and Novel H1N1 Virus Infection

The July 31st WHO statement also contained information on the increased risk of serious illness among pregnant women infected with novel H1N1 virus:

> Research conducted in the USA and published 29 July in *The Lancet* has drawn attention to an increased risk of severe or fatal illness in pregnant women when infected with the H1N1 pandemic virus.
>
> Several other countries experiencing widespread transmission of the pandemic virus have similarly reported an increased risk in pregnant women, particularly during the second and third trimesters of pregnancy. An increased risk of fetal death or spontaneous abortions in infected women has also been reported.
>
> Evidence from previous pandemics further supports the conclusion that pregnant women are at heightened risk.
>
> While pregnant women are also at increased risk during epidemics of seasonal influenza, the risk takes on added importance in the current pandemic, which continues to affect a younger age group than that seen during seasonal epidemics.
>
> (See Jamieson DJ, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *The Lancet*, Early Online Publication, July 29, 2009. The abstract is available at http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)61304-0/abstract.)

The Centers for Disease Control and Prevention (CDC) recommends early treatment with influenza antiviral medication for pregnant women with suspected influenza illness. Because of its systemic activity, the current drug of choice for treatment of pregnant women is oseltamivir. Recommended duration of treatment is five days. Treatment should not be delayed while waiting for the results of viral testing. As is recommended for other persons who are treated, antiviral treatment should be initiated as soon as possible after the onset of influenza symptoms, with benefits expected to be greatest if started within 48 hours of onset, based on data from studies of seasonal influenza. However, data from studies on seasonal influenza indicate benefit for hospitalized patients even if treatment is started more than 48 hours after onset. Thus, antiviral medications are recommended for high risk persons, including pregnant women, presenting for care more than 48 hours after illness onset, particularly for those who require hospitalization.

Complete clinical management guidelines for pregnant women are available from CDC at http://www.cdc.gov/h1n1flu/clinician_pregnant.htm. Included here is the recommendation that fever in pregnant women should be treated because of the risk that hyperthermia appears to pose to the fetus. Acetaminophen appears to be the best option for treatment of fever during pregnancy.

CDC additionally states that post-exposure antiviral chemoprophylaxis can be considered for pregnant women who are close contacts of persons with suspected or laboratory-confirmed novel H1N1 virus infection. For more information, go to http://www.cdc.gov/h1n1flu/clinician_pregnant.htm.

Related guidance from CDC, entitled "Considerations Regarding Novel H1N1 Flu Virus in Obstetric Settings", is found at http://www.cdc.gov/h1n1flu/guidance/obstetric.htm.

As more information becomes available, these guidelines may be modified. Medical professionals caring for pregnant women and newborns are encouraged to check these websites periodically for updates.

Information on Rapid Influenza Diagnostic Tests

CDC has recently released a document entitled "Interim Guidance for the Detection of Novel Influenza A Virus Using Rapid Influenza Diagnostic Tests", which provides information on these tests, including their limitations, to help guide their proper use and interpretation. Go to http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm.

New Guidance on the Amount of Time Persons with Influenza-Like Illness Should Remain at Home

CDC now recommends that people with influenza-like illness remain at home (except when necessary to seek required medical care) until at least 24 hours after they are free of fever (100° F [37.8°C]), or signs of a fever without the use of fever-reducing medications (http://www.cdc.gov/h1n1flu/guidance/exclusion.htm). Note that this is a change from the previous recommendation that ill persons stay home for 7 days after illness onset or until 24 hours after the resolution of symptoms, whichever was longer.

Keeping people with a fever at home may reduce the number of other individuals who get infected, since elevated temperature is associated with increased shedding of influenza virus. CDC recommends this exclusion period regardless of whether or not antiviral medications are used.

This new recommendation applies to camps, schools, businesses, mass gatherings, and other community settings where the majority of people are not at increased risk for influenza complications.

This new guidance does not apply to health care settings where the exclusion period should be continued for 7 days from symptom onset or until the resolution of symptoms, whichever is longer; see http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm for updates about the health care setting.

More guidance for patients is available from CDC at http://www.cdc.gov/h1n1flu/guidance/#a6.

Novel H1N1 Virus Vaccine

CDC's Advisory Committee on Immunization Practices (ACIP) met July 29 to determine who should receive vaccine against novel H1N1 virus when it becomes available, and to determine which groups of the population should be prioritized if the vaccine is initially available in limited quantities. Recommendations from this meeting are summarized at http://www.cdc.gov/h1n1flu/vaccination/acip.htm and http://www.cdc.gov/media/pressrel/2009/r090729b.htm.

Current information for medical providers on the manufacture of novel H1N1 vaccine, and the anticipated delivery system that will be utilized once it becomes available, is found at http://www.cdc.gov/h1n1flu/vaccination/provider/preparing.htm.

Guidance on novel H1N1 vaccination for public health officials is available from CDC at http://www.cdc.gov/h1n1flu/vaccination/statelocal/.

Links to comprehensive information for medical providers on novel H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

As new information becomes available, the Missouri Department of Health and Senior Services (DHSS) will issue additional Health Updates.

Questions on novel H1N1 influenza should be directed to your local public health agency, or to DHSS' Bureau of Communicable Disease Control and Prevention at 573/751-6113, or 866-628-9891.

Health Update:

Update: Shortage of Erythromycin Ophthalmic Ointment for Prophylaxis of Ophthalmia Neonatorum

September 10, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

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Health Update
September 10, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **Update: Shortage of Erythromycin Ophthalmic Ointment for Prophylaxis of Ophthalmia Neonatorum**

The Centers for Disease Control and Prevention (CDC) and the Missouri Department of Health and Senior Services (DHSS) recently received reports of a shortage of erythromycin (0.5%) ophthalmic ointment, which is the recommended prophylaxis for ophthalmia neonatorum. On September 4, 2009, DHSS issued a Health Advisory, entitled "Shortage of Erythromycin Ophthalmic Ointment for Prophylaxis of Ophthalmia Neonatorum", which contained guidance from CDC for responding to this situation (http://www.dhss.mo.gov/BT_Response/HAds/HAd9-4-09.pdf).

CDC has now revised their guidance to include not only recommendations for securing supplies of erythromycin ophthalmic ointment, but also recommendations for the use of other ophthalmic solutions or ointments "for extreme situations where erythromycin ophthalmic ointment is not available." An alternative or additional approach provided in the guidance is to test the mother for gonorrhea and chlamydia prior to delivery in order to identify exposed infants. Empiric treatment is recommended for infants exposed to gonorrhea; monitoring for development of symptoms prior to initiating treatment is recommended for infants exposed to chlamydia. The revised CDC guidance is available at:
http://www.cdc.gov/std/treatment/2006/erythromycinOintmentShortage.htm.

Additional changes to this guidance may occur in the future. Providers are strongly encouraged to periodically check CDC's STD Treatment Guidelines Web site at http://www.cdc.gov/std/treatment/default.htm for possible further revisions.

Contact the FDA drug shortage e-mail account (drugshortages@fda.hhs.gov) with additional inquiries about the shortage. Questions can also be directed to DHSS's Bureau of HIV, STD, and Hepatitis at 573/751-6439, or 800/392-0272 (24/7).

Health Update:

2009 H1N1 Influenza Update 10: Reporting Laboratory-Confirmed Cases of Influenza, and Outbreaks of Influenza-Like Illness, to Public Health Officials

September 11, 2009

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Health Update
September 11, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 10: Reporting Laboratory-Confirmed Cases of Influenza, and Outbreaks of Influenza-Like Illness, to Public Health Officials**

The Missouri Department of Health & Senior Services (DHSS) reminds clinicians of the importance of reporting all laboratory-confirmed influenza cases, as well as all outbreaks of influenza-like illness (ILI), to their local public health agency (LPHA).

Reporting Laboratory-Confirmed Influenza Cases

All laboratory-confirmed influenza cases, including those caused by the 2009 H1N1 influenza virus, are reportable under the Missouri Code of State Regulations (19 CSR 20-20.020). These cases are to be reported in an aggregated format on a weekly basis. A form has been developed for medical providers to use in making these reports, and it can be obtained by going to http://www.dhss.mo.gov/Influenza/ReportersWorksheet.pdf, or by contacting your LPHA. (Information for contacting individual LPHAs is available at http://www.dhss.mo.gov/LPHA/LPHAs.html. For a listing of all reportable diseases/conditions, go to http://www.dhss.mo.gov/CommunicableDisease/reportablediseaselist2.pdf.)

A number of different laboratory diagnostic tests can be used for detecting the presence of influenza viruses in respiratory specimens, including direct antigen detection tests, virus isolation in cell culture, or detection of influenza-specific RNA by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR).

In addition to the tests listed above, many health care providers use rapid influenza diagnostic tests (RIDTs), which are antigen detection tests that detect influenza viral nucleoprotein antigen. These tests meet the requirements of the disease reporting rule and positive results should be reported. RIDTs can provide results within 30 minutes or less. Thus, results are available in a clinically relevant time period to inform clinical decisions.

Commercially available RIDTs can either:

1. Detect and distinguish between influenza A and B viruses;
2. Detect both influenza A and B, but not distinguish between influenza A and B viruses; or,
3. Detect only influenza A viruses

None of the current FDA-approved RIDTs can distinguish between influenza A virus subtypes. When reporting a positive RIDT result, indicate the specific test finding (e.g., RIDT positive for influenza A, or RIDT positive for influenza B). Do not report a RIDT positive for influenza A as a positive test for 2009 H1N1 influenza virus, even if this is strongly suspected. Guidance for using RIDTs in the context of the 2009 H1N1 influenza pandemic is available from the Centers for Disease Control and Prevention (CDC) at http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm.

In summary, positive results from any of the following test types should be reported to your LPHA:

- Direct antigen detection tests
- Virus isolation in cell culture
- rRT-PCR
- RIDTs

Reporting Outbreaks of Influenza-Like Illness (ILI)

The Missouri Code of State Regulations (19 CSR 20-20.020) also requires the reporting of outbreaks of ILI. ILI is defined as a fever greater than 100^0 F, accompanied by cough or sore throat.

Outbreaks can be reported to your LPHA, or to DHSS at 800/392-0272 (24/7). Reports should be made within one day of first knowledge or suspicion. Prompt reporting of outbreaks will help public health officials quickly intervene to slow further transmission in the community.

2009 H1N1 Influenza

The 2009 H1N1 influenza virus is circulating throughout the state, and DHSS strongly encourages clinicians to continue reporting laboratory-confirmed cases caused by this virus (i.e., cases with positive results from a test that is specific for the 2009 H1N1 virus).

A summary of the Missouri State Public Health Laboratory's policies for 2009 H1N1 influenza virus testing is found in the Appendix on the next page.

Comprehensive information and guidance on 2009 H1N1 influenza for medical professionals is available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Questions on 2009 H1N1 influenza, or on any issue related to influenza reporting, can be directed to your LPHA, or to DHSS' Bureau of Communicable Disease Control and Prevention at 573-751-6113 or 866-628-9891.

Appendix

Missouri Department of Health and Senior Services

2009 H1N1 Influenza Laboratory Testing

September 10, 2009

The primary responsibility of the Missouri State Public Health Laboratory (MSPHL) during influenza epidemics and pandemics is surveillance and epidemiological testing in support of early detection, public health response and control measures, and measuring the progress and "character" of a pandemic wave(s) as it progresses at the community and state level. In the early stages of a pandemic, this involves a surge in diagnostic testing to detect cases and monitor the spread of the virus. As a pandemic evolves, the public health need to identify every case diminishes as do resources.

Missouri is beyond the early stages of the 2009 H1N1 Influenza pandemic and is currently experiencing sporadic outbreaks in congregate settings such as schools and daycares. It appears likely that infections with this virus are occurring throughout the state, although their exact number cannot be estimated.

Following advice from the World Health Organization and Centers for Disease Control and Prevention, the MSPHL is currently following a testing protocol that is consistent with seasonal influenza practices and is not accepting routine specimens for novel H1N1 influenza virus testing. MSPHL will only be performing testing for this virus under the following circumstances:

1. Specimens submitted by Influenza Sentinel Providers, or

2. Specimens submitted for epidemiological investigation purposes (i.e., as part of an outbreak being investigated by DHSS, local public health agencies, and/or CDC).

The MSPHL will not perform testing on hospitalized patients, unless the testing is deemed to be of public health significance by DHSS (e.g., epidemiologically linked cases, cases with similar demographics, etc.). Commercial laboratory testing is available for routine testing of hospitalized patients.

[Note for Influenza Sentinel Providers: Sentinel Providers have returned to their traditional off-season testing protocol. DHSS requests that a minimum of three specimens be sent from each Sentinel Provider during the period from June 1 through September 30. Sentinel Providers should also submit their weekly office data to the Influenza Sentinel Physicians Surveillance Network Database.]

For patients who do not meet the above criteria, commercial laboratory testing is available.

If you have any questions, please contact the Bureau of Communicable Disease Control and Prevention at (573) 751-6113.

Health Update:

2009 H1N1 Influenza Update 11: Antiviral Medication and Influenza Testing Issues

September 25, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov

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Health Update
September 25, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 11: Antiviral Medication and Influenza Testing Issues**

This Health Update provides: 1) information on potential confusion associated with use of the oral dosing dispenser provided with Tamiflu suspension; 2) reports of limited supplies of Tamiflu suspension; 3) updated guidance on the use of antiviral drugs; 4) updated antiviral medication recommendations for obstetric care providers; and 5) information on possible positive rapid influenza diagnostic test results in persons who have recently received live, attenuated influenza vaccine.

Potential Confusion Associated With Use of the Oral Dosing Dispenser Provided With Tamiflu Oral Suspension

An issue that physicians and pharmacists may face is the need to ensure that the units of measure on the dosing dispenser and the dosing instructions match. An oral dosing dispenser with 30 mg, 45 mg, and 60 mg graduations of Tamiflu is provided in the packaging for the manufacturer's product rather than graduations in milliliters (mL) or teaspoons (tsp). This can lead to patient or caregiver confusion and dosing errors. When dispensing commercially manufactured Tamiflu oral suspension, pharmacists should ensure the units of measure on the dosing instructions match the dosing device provided. If prescription instructions specify administration using mL or tsp, then the device included in the Tamiflu product package should be removed and replaced with an appropriate measuring device, such as an oral syringe if the prescribed dose is in milliliters (mL). When dispensing Tamiflu oral suspension for children younger than 1 year of age, the oral dosing dispenser that is included in the product package should always be removed. Pharmacists and health care providers should provide an oral syringe that is capable of accurately measuring the prescribed milliliter (mL) dose, and counsel the caregiver how to administer the prescribed dose. Oseltamivir is authorized for emergency use in children younger than 1 year of age under an Emergency Use Authorization (EUA) issued by the Food and Drug Administration (FDA). For the EUA, see http://www.cdc.gov/h1n1flu/eua/pdf/tamiflu-hcp.pdf.

Limited Supplies of Tamiflu Oral Suspension

The Food and Drug Administration (FDA) and Roche (maker of Tamiflu) have acknowledged that commercial and stockpiled supplies of Tamiflu oral suspension are limited. **Limited supplies** of Tamiflu oral suspension made available to Missouri from the Strategic National Stockpile (SNS) and included in local public health agencies' antiviral medication planning can be used **for treatment** when other community resources have been exhausted.

If pediatric formulations of Tamiflu are not available, pharmacists may compound Tamiflu 75 mg capsules into an oral suspension onsite. For the FDA -approved instructions for the emergency compounding of an oral suspension from Tamiflu 75mg capsules, see the FDA approved manufacturer package insert for oseltamivir (Tamiflu) at: http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM147992.pdf.

Compounding an oral suspension from Tamiflu 75mg capsules provides an alternative when commercially manufactured oral suspension formulation is not readily available. Tamiflu capsules 75 mg may be compounded using either of two vehicles: Cherry Syrup (Humco®) or Ora-Sweet® SF (sugar-free) (Paddock Laboratories). Other supplies needed to

compound include mortar and pestle and amber glass or amber polyethyleneterephthalate (PET) bottle.

In addition, for children who may not be able to swallow capsules, Tamiflu (30mg, 45mg, and 75mg) capsules may be opened and mixed with sweetened liquids, such as regular or sugar-free chocolate syrup, if oral suspension is not available.

Updated Guidance on the Use of Antiviral Drugs for Treatment and Prophylaxis of Influenza

On September 22, 2009, CDC updated its recommendations for the use of antiviral drugs for treatment and prophylaxis of 2009 H1N1 influenza and seasonal influenza. The updated recommendations are available at http://www.cdc.gov/h1n1flu/recommendations.htm, and are intended to help clinicians prioritize the use of antiviral medications for treatment and prevention.

As in earlier recommendations, the priority for use of antiviral medications continues to be in people with more severe illness, such as people hospitalized with influenza, and people at increased risk of influenza-related complications. CDC notes that as with any medical decision making, clinical judgment is an essential factor in making decisions about treatment with antiviral medications.

DHSS strongly emphasizes the importance of a judicial use of antiviral medications in order to prevent emergence of antiviral resistance, and to ensure that the existing limited supplies of antiviral medications are being used in the most effective way possible.

Key points from the guidance include the following. All clinicians who provide care for influenza patients and their contacts are strongly encouraged to read the complete document (http://www.cdc.gov/h1n1flu/recommendations.htm).

Treatment

- Most healthy persons who develop an illness consistent with influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment. However, persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age.
- Treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) is recommended for all persons with suspected or confirmed influenza requiring hospitalization.
- Early empiric treatment with oseltamivir or zanamivir should be considered for persons with suspected or confirmed influenza who are at higher risk for complications including:
    - **Children younger than 2 years old;**
    - **Persons aged 65 years or older;**
    - **Pregnant women;**
    - **Persons of any age with certain chronic medical or immunosuppressive conditions (see http://www.cdc.gov/h1n1flu/recommendations.htm); and,**
    - **Persons younger than 19 years of age who are receiving long-term aspirin therapy**

  Clinical judgment should be used in deciding whether outpatients with risk factors for influenza-related complications require treatment.
- Children 2 years to 4 years old are more likely to require hospitalization or urgent medical evaluation for influenza compared with older children, although the risk is much lower than for children younger than 2 years old. Children aged 2 years to 4 years without high risk conditions and with mild illness do not necessarily require antiviral treatment.
- Treatment, when indicated, should be initiated as early as possible (and should not wait on laboratory results) because studies show that treatment initiated early (i.e., within 48 hours of illness onset) is more likely to provide benefit. However, some studies of hospitalized patients with seasonal influenza treated with oseltamivir have suggested benefit, including reductions in mortality or duration of hospitalization, even for patients whose treatment was started more than 48 hours after illness onset.
- The recommended duration of treatment is five days. Hospitalized patients with severe infections (such as those with prolonged infection or who require intensive care unit admission) might require longer treatment courses. Some experts have advocated use of increased (doubled) doses of oseltamivir for

some severely ill patients, although there are no published data demonstrating that higher doses are more effective.

- Oseltamivir use for children younger than 1 year old was recently authorized by FDA under an EUA (see http://www.cdc.gov/h1n1flu/eua/tamiflu.htm). These EUA provisions apply only when the product is provided in accordance with the local public health authority's response plans. Dosing for children younger than 1 year old is age-based in the EUA guidance (see the dosing recommendations at http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM153546.pdf). However, some experts who are currently conducting studies on oseltamivir use in this age group prefer weight based dosing for this age group, particularly for premature or underweight infants.

Chemoprophylaxis

- Consideration for chemoprophylaxis should generally be reserved for persons at higher risk for influenza-related complications who have had contact with someone likely to have been infected with influenza. However, early treatment is an emphasized alternative to chemoprophylaxis after a suspected exposure. Household or close contacts (with risk factors for influenza complications) of confirmed or suspected cases can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their health care provider for evaluation and possible early treatment if clinical signs or symptoms develop.

  Close contact, for the purposes of this guidance, is defined as having cared for or lived with a person who is a confirmed, probable, or suspected case of influenza, or having been in a setting where there was a high likelihood of contact with respiratory droplets and/or body fluids of such a person. Examples of close contact include sharing eating or drinking utensils, physical examination, or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person or sitting across from a symptomatic patient in a waiting room or office.

- Post-exposure chemoprophylaxis with either oseltamivir or zanamivir can also be considered for health care personnel, public health workers, or first responders who have had a recognized, unprotected close contact exposure to a person with known or suspected 2009 H1N1 or seasonal influenza.
- For antiviral chemoprophylaxis of 2009 H1N1 influenza virus infection, either oseltamivir or zanamivir is recommended. Duration of post-exposure chemoprophylaxis is 10 days after the last known exposure to 2009 H1N1 influenza.
- Antiviral agents should not be used for post-exposure chemoprophylaxis in healthy children or adults based on potential exposures in the community, school, camp, or other settings. Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person. Chemoprophylaxis is not indicated when contact occurred before or after, but not during, the ill person's infectious period.

  For the purposes of this guidance, the infectious period for influenza is defined as one day before until 24 hours after fever ends.

- Patients receiving chemoprophylaxis should be encouraged to promptly seek medical evaluation if they develop a febrile respiratory illness that might indicate influenza.
- Oseltamivir was authorized for use for chemoprophylaxis under the EUA for children younger than 1 year of age, subject to the terms and conditions of the EUA. Age-based dosing recommendations are provided in the fact sheets included with the EUA letter of authorization (available at http://www.cdc.gov/h1n1flu/eua/); dosing recommendations are also available at http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM153546.pdf. Note that weight-based dosing is an alternative preferred by some experts who are currently conducting studies of oseltamivir use in this age group.
- Oseltamivir-resistant 2009 H1N1 viruses have been identified, typically among persons who develop illness while receiving oseltamivir for chemoprophylaxis or immunocompromised patients with influenza who are being treated. These findings underscore the importance of careful and limited use of antiviral medications for chemoprophylaxis and the need for persons taking antiviral medications to continue to follow recommendations for hand and respiratory hygiene to prevent the spread of antiviral-resistant viruses.

Patients receiving treatment should be advised that they remain potentially infectious to others while on treatment. Despite treatment with antiviral agents, including treatment with the neuraminidase inhibitors, patients may continue to shed influenza virus for up to four or more days after beginning therapy. Therefore, patients should continue good hand washing and respiratory hygiene practices during the entire period on therapy to prevent the transmission of virus to close contacts. See *Taking Care of a Sick Person in Your Home* at http://www.cdc.gov/h1n1flu/guidance_homecare.htm, and *Home Care Guidance: Physician Directions to Patient/Parent* at http://www.cdc.gov/h1n1flu/guidance_homecare_directions.htm.

Recommendations for Obstetric Health Care Providers Related to Use of Influenza Antiviral Medications

Pregnant women are at higher risk for severe complications and death from influenza, including both 2009 H1N1 influenza and seasonal influenza. CDC has recently issued updated recommendations for obstetric health care providers on the use of antiviral medications (http://www.cdc.gov/H1N1flu/pregnancy/antiviral_messages.htm). Key points from the recommendations include the following. All clinicians who provide care for pregnant women are strongly encouraged to read the complete document.

Treatment

- Treatment with oseltamivir (Tamiflu) or zanamivir (Relenza) is recommended for pregnant women with suspected or confirmed influenza and can be taken during any trimester of pregnancy.
- Oseltamivir and zanamivir are "Pregnancy Category C" medications, indicating that no clinical studies have been conducted to assess the safety of these medications for pregnant women. However, CDC states the available risk-benefit data indicate pregnant women with suspected or confirmed influenza should receive prompt antiviral therapy. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use.
- For treatment of pregnant women with suspected or confirmed influenza, oseltamivir is currently preferred because of its systemic absorption.
- Fever in pregnant women should be treated because of the risk that it appears to pose to the fetus. Acetaminophen appears to be the best option for treatment of fever during pregnancy.

Chemoprophylaxis

- Post-exposure chemoprophylaxis can be considered for pregnant women who have had contact with someone likely to have been infectious with influenza. The drug of choice for chemoprophylaxis of pregnant women is less clear. Zanamivir may be the preferable antiviral for chemoprophylaxis of pregnant women because of its limited systemic absorption. However, respiratory complications that may be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems. For these women, oseltamivir is a reasonable alternative.
- Early treatment is an alternative to chemoprophylaxis for some pregnant women who have had contact with someone likely to have been infectious with influenza. Clinical judgment is an important factor in treatment decisions.

Rapid Influenza Diagnostic Tests and Live, Attenuated Influenza Vaccine

Rapid influenza diagnostic tests (RIDTs) are widely used, and last month CDC issued guidance for the detection of 2009 H1N1 virus using these tests (http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm). Clinicians should be aware that if a person receives live, attenuated influenza vaccine (LAIV) and then, within the next few days, develops an influenza-like illness and has a rapid influenza test, this test may be positive because it is detecting the presence of vaccine virus or, alternatively, it could be detecting a wild-type influenza virus. In studies that have looked at vaccine virus shedding in LAIV recipients (using RIDTs and other, more sensitive, tests such as culture and PCR), none of the participants had detectable virus beyond 10 days after receipt of the vaccine. (*MMWR* 2008;57[RR-7]:17-18.)

Links to comprehensive information and guidance on 2009 H1N1 influenza for medical professionals is available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Questions on 2009 H1N1 influenza can be directed to your local public health agency, or to DHSS' Bureau of Communicable Disease Control and Prevention at 573-751-6113 or 866-628-9891.

Health Update:

2009 H1N1 Influenza Update 12: Use of H1N1 Influenza Vaccine Containing Thimerosal, Missouri's H1N1 InfoLine, Antiviral Drug Use, Clinical Features of Severe Cases, Triage Algorithms, H1N1 Influenza Vaccine

October 23, 2009

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Health Update
October 23, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 12: Use of H1N1 Influenza Vaccine Containing Thimerosal, Missouri's H1N1 InfoLine, Antiviral Drug Use, Clinical Features of Severe Cases, Triage Algorithms, H1N1 Influenza Vaccine**

This Health Update provides: 1) information on the use of H1N1 influenza vaccine containing thimerosal in pregnant women and young children; 2) announcement of Missouri's H1N1 InfoLine; 3) updated information on the use of antiviral drugs for influenza treatment and prophylaxis; 4) information on the clinical features of severe cases of 2009 H1N1 influenza; 5) links to triage algorithms for adults and children with influenza-like illness; and 6) information and guidance on 2009 H1N1 influenza vaccine.

Use of 2009 H1N1 Influenza Vaccine Containing Thimerosal in Pregnant Women and Young Children

Margaret Donnelly, director of the Department of Health and Senior Services (DHSS), granted an exemption Thursday, October 22, 2009, to the requirements of 191.235, RSMo. This exemption allows pregnant women and parents of children less than three years old to choose whether to receive 2009 H1N1 influenza vaccine containing thimerosal. Director Donnelly determined that a shortage of preservative-free vaccine was preventing pregnant women and young children from obtaining the new H1N1 vaccine.

Donnelly's action temporarily sets aside the statute that prohibited pregnant women and children under three from receiving vaccine with this preservative. The waiver will remain in effect until the shortage no longer exists.

Under the exemption, pregnant women and families of children younger than three years old will be able to decide whether to receive 2009 H1N1 influenza vaccine that contains small traces of mercury-based preservative.

Information on thimerosal in influenza vaccine is available from the Centers for Disease Control and Prevention (CDC) at http://www.cdc.gov/flu/about/qa/thimerosal.htm.

Missouri's H1N1 InfoLine

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).

Use of Antiviral Drugs for Treatment and Prophylaxis of Influenza

DHSS and the Board of Registration for the Healing Arts have recently sent a letter to medical providers reminding them of the importance of the appropriate use of antiviral medications for the treatment and prophylaxis of influenza. Proper use of these drugs is necessary in order to ensure that adequate amounts will remain available for persons who

will benefit most from their use, and so that the potential development of widespread antiviral resistance to these medications can be avoided. The medical providers' letter, and an accompanying summary of updated antiviral guidance from CDC, are shown in the Appendix to this document, and are also available at http://www.dhss.mo.gov/BT_Response/SwineFlu/PhysicianLetterandGuidanceSummary.pdf. The CDC guidance (which applies to the treatment and prophylaxis of both 2009 H1N1 and seasonal influenza virus infections) is found at http://www.cdc.gov/h1n1flu/recommendations.htm.

Regarding treatment, the CDC guidance states that most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment. However, persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age. Antiviral treatment is also recommended for all persons with suspected or confirmed influenza requiring hospitalization. In addition, early empiric antiviral treatment should be considered for persons with suspected or confirmed influenza who are at higher risk for complications (these are listed in the guidance document). For antiviral treatment of 2009 H1N1 virus infection, either oseltamivir or zanamivir is recommended. Both the CDC guidance document and a more recent CDC statement (http://www.cdc.gov/H1N1flu/HAN/101909.htm) emphasize that when treatment is indicated in a patient with suspected influenza, health care providers should initiate empiric antiviral treatment as soon as possible. Waiting for laboratory confirmation of influenza to begin treatment with antiviral drugs is not necessary. Patients with a negative rapid influenza diagnostic test should be considered for treatment if clinically indicated because a negative rapid influenza test result does not rule out influenza virus infection. The sensitivity of rapid influenza diagnostic tests for 2009 H1N1 virus can range from 10% to 70%, indicating that false negative results occur frequently.

The CDC guidance additionally states that consideration for antiviral chemoprophylaxis (with either oseltamivir or zanamivir) should generally be reserved for persons at higher risk for influenza-related complications who have had contact with someone likely to have been infected with influenza. However, early treatment is an emphasized alternative to chemoprophylaxis after a suspected exposure. Antiviral agents should not be used for post-exposure chemoprophylaxis in healthy children or adults based on potential exposures in the community, school, camp, or other settings. Also, chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person.

In addition to the updated antiviral guidance, CDC has recently issued supplemental recommendations for health care providers of children and adolescents on the use of antiviral medications for treatment and chemoprophylaxis. These recommendations are available at http://www.cdc.gov/h1n1flu/recommendations_pediatric_supplement.htm. CDC has also issued guidance on influenza antiviral treatment of pregnant women, which is available at http://www.cdc.gov/h1n1flu/clinician_pregnant.htm.

CDC has recently developed a new website which provides safety information on antiviral drugs; it can be accessed at http://www.cdc.gov/H1N1flu/antivirals/safety_info.htm.

Links to more information on antiviral drugs are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html (see the Antiviral Drugs section).

Clinical Features of Severe Cases of Pandemic Influenza

On October 14-16, the World Health Organization (WHO) hosted a three-day meeting in Washington, DC, to gather information about the clinical features and management of patients with 2009 H1N1 influenza. A brief report is found at http://www.who.int/csr/disease/swineflu/notes/h1n1_clinical_features_20091016/en/index.html. Key points include the following:

- The meeting confirmed that the overwhelming majority of persons worldwide infected with the new H1N1 virus continue to experience uncomplicated influenza-like illness, with full recovery within a week, even without medical treatment.

- Concern is now focused on the clinical course and management of small subsets of patients who rapidly develop very severe progressive pneumonia. In these patients, severe pneumonia is often associated with failure of other organs, or marked worsening of underlying asthma or chronic obstructive airway disease.

- Treatment of these patients is difficult and demanding, strongly suggesting that emergency rooms and intensive care units will experience the heaviest burden of patient care during the pandemic.

- Primary viral pneumonia is the most common finding in severe cases and a frequent cause of death. Secondary bacterial infections have been found in approximately 30% of fatal cases. Respiratory failure and refractory shock have been the most common causes of death.

- The clinical picture in severe cases is strikingly different from the disease pattern seen during epidemics of seasonal influenza. While people with certain underlying medical conditions, including pregnancy, are known to be at increased risk, many severe cases occur in previously healthy young people. In these patients, predisposing factors that increase the risk of severe illness are not presently understood.

- In severe cases, patients generally begin to deteriorate around 3 to 5 days after symptom onset. Deterioration is rapid, with many patients progressing to respiratory failure within 24 hours, requiring immediate admission to an intensive care unit. Upon admission, most patients need immediate respiratory support with mechanical ventilation. However, some patients do not respond well to conventional ventilatory support, further complicating the treatment.

- There is a growing body of evidence that prompt treatment with the antiviral drugs, oseltamivir or zanamivir, reduces the severity of illness and improves the chances of survival. These findings strengthen previous WHO recommendations for early treatment with these drugs for patients who meet treatment criteria, even in the absence of a positive confirmatory test.

- In addition to pneumonia directly caused by replication of the virus, evidence shows that pneumonia caused by co-infection with bacteria can also contribute to a severe, rapidly progressive illness. Bacteria frequently reported include *Streptococcus pneumoniae* and *Staphylococcus aureus*, including methicillin-resistant strains in some cases. As these bacterial co-infections are more frequent than initially recognized, clinicians stressed the need to consider empiric antimicrobial therapy for community-acquired pneumonia as an early treatment.

- Participants agreed that the risk of severe or fatal illness is highest in three groups: pregnant women, especially during the third trimester of pregnancy, children younger than 2 years of age, and people with chronic lung disease, including asthma. Neurological disorders can increase the risk of severe disease in children.

- Evidence presented during the meeting further shows that disadvantaged populations, such as minority groups and indigenous populations, are disproportionately affected by severe disease.

- Although the exact role of obesity is poorly understood at present, obesity and especially morbid obesity have been present in a large portion of severe and fatal cases. Obesity has not been recognized as a risk factor in either past pandemics or seasonal influenza.

Triage Algorithms For Adults and Children With Influenza-Like Illness

CDC, in collaboration with Emory University School of Medicine, has developed a triage algorithm for adults (>18 years of age) with influenza-like illness (ILI). This algorithm was designed to assist physicians and those under their supervision in identifying indicators of and responses to symptoms of flu-like illness. It is available at http://www.cdc.gov/h1n1flu/clinicians/pdf/adultalgorithm.pdf.

CDC and the American Academy of Pediatrics (AAP) have developed a triage algorithm for children (≤18 years of age) with ILI. This algorithm is intended for use by physicians and those under their direct supervision to help in discussions and providing advice to parents or other caregivers of ill children regarding seeking medical care for an ILI. It is available at http://www.cdc.gov/h1n1flu/clinicians/pdf/childalgorithm.pdf.

2009 H1N1 Influenza Vaccine

Four influenza vaccine manufacturers have received approval from the Food and Drug Administration (FDA) for their 2009 H1N1 monovalent influenza vaccines. Both live, attenuated and inactivated influenza vaccine formulations have been approved. Initial supplies of these vaccines are now coming into Missouri, and more will become available in the coming weeks. See http://www.dhss.mo.gov/BT_Response/_provider_listing.html for current information on 2009 H1N1 and seasonal influenza vaccines in Missouri.

Because the initially available quantities of these vaccines are limited, they should, at this time, be given to persons in the following priority groups (note that the order of the target groups does not indicate priority):

- **Pregnant women,**
- **Persons who live with or provide care for infants aged <6 months (e.g., parents, siblings, and daycare providers),**
- **Health-care and emergency medical services personnel who have direct contact with patients or infectious material,**
- **Children aged 6 months - 4 years, and**
- **Children and adolescents aged 5 - 18 years who have medical conditions that put them at higher risk for influenza-related complications. These conditions include chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, cognitive, neurologic/neuromuscular, hematologic, or metabolic disorders (including diabetes mellitus); or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus).**

Once vaccine availability increases (hopefully within the next few weeks), the following five groups will then be prioritized to receive the vaccine (note that the order of the target groups does not indicate priority):

- Pregnant women,
- People who live with or provide care for infants younger than 6 months of age (e.g., parents, siblings, and day care providers),
- Health care and emergency medical services personnel,
- People 6 months through 24 years of age, and,
- People 25 years through 64 years of age who have certain medical conditions that put them at higher risk for influenza-related complications.

Then, when vaccination programs and providers are meeting the demand for vaccine among persons in these target groups, vaccination should be expanded to all persons aged 25-64 years.

Finally, once demand for vaccine among younger age groups is being met, vaccination should be expanded to all persons aged ≥65 years.

Information and guidance on 2009 H1N1 influenza vaccine is available from CDC and FDA, and includes:

- Update on Influenza A (H1N1) 2009 Monovalent Vaccines (CDC)
  http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5839a3.htm
- Vaccine Information Statements: 2009 H1N1 Influenza Vaccine (CDC)
  http://www.cdc.gov/vaccines/pubs/vis/default.htm#h1n1live

- H1N1 Clinicians Questions and Answers (CDC)
  http://www.cdc.gov/h1n1flu/vaccination/clinicians_qa.htm
- 10 FAQs for Immunization Programs and Providers (CDC)
  http://www.cdc.gov/H1N1flu/vaccination/top10_faq.htm
- 2009 H1N1 Influenza Vaccine and Pregnant Women: Information for Healthcare Providers (CDC)
  http://www.cdc.gov/h1n1flu/vaccination/providers_qa.htm
- Influenza A (H1N1) 2009 Monovalent (FDA) (Includes links to the package insert for each vaccine.)
  http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm181950.htm

More information on 2009 H1N1 vaccine is available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html (see the Vaccine section).

APPENDIX

Missouri Department of Health and Senior Services
P.O. Box 570, Jefferson City, MO 65102-0570 Phone: 573-751-6400 FAX: 573-751-6010
RELAY MISSOURI for Hearing and Speech Impaired 1-800-735-2966 VOICE 1-800-735-2466

Margaret T. Donnelly
Director

Jeremiah W. (Jay) Nixon
Governor

October 21, 2009

To All Missouri Medical Physicians:

The Missouri Department of Health and Senior Services (DHSS) and the Board of Registration for the Healing Arts wish to emphasize the importance of the appropriate use of antiviral medications for the treatment and prophylaxis of influenza in order to prevent emergence of antiviral resistance, and to ensure that the existing limited supplies of antiviral drugs are being used in the most effective way possible.

2009 H1N1 influenza virus infections are spreading widely throughout the United States, including Missouri. Most infected persons have uncomplicated, typical influenza-like illness and do not require medical care. However serious illnesses and deaths have occurred, and certain groups of persons appear to be at increased risk of complications. Antiviral medications are available for influenza treatment and prophylaxis, but proper use of these drugs is important in order to ensure that adequate amounts will remain available for persons who will most benefit from their use, and so that the widespread occurrence of antiviral resistance can be avoided.

Shortages of oseltamivir (Tamiflu) oral suspension have recently been reported, and there are ongoing concerns that the widespread resistance to oseltamivir currently seen with seasonal H1N1 influenza viruses could also emerge in 2009 H1N1 influenza viruses. A relatively small number of oseltamivir-resistant 2009 H1N1 viruses have been identified, typically among persons who develop illness while receiving oseltamivir for chemoprophylaxis or immunocompromised patients with influenza who are being treated. These events particularly underscore the importance of the appropriate use of antiviral medications for treating individuals with known or suspected influenza, and the careful and limited use of these drugs for chemoprophylaxis.

The Centers for Disease Control and Prevention (CDC) has issued guidance for the use of antiviral medications for treatment and prophylaxis of influenza. Physicians are strongly encouraged to become familiar with these recommendations, and to incorporate them into their clinical decision-making. This guidance will likely be updated periodically, and the current version can be found at http://www.cdc.gov/h1n1flu/recommendations.htm. Also note that this guidance applies to the treatment and prophylaxis of both 2009 H1N1 and seasonal influenza virus infections. A summary of the guidance is attached.

Sincerely,

Margaret T. Donnelly

Margaret T. Donnelly
Director

Summary of Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza

Centers for Disease Control and Prevention (CDC)
October 16, 2009

See http://www.cdc.gov/h1n1flu/recommendations.htm for the complete set of recommendations. In addition, supplemental recommendations for health care providers of children and adolescents have also been issued and are found at http://www.cdc.gov/h1n1flu/recommendations_pediatric_supplement.htm.

Treatment

- Influenza antiviral medications can reduce the severity and duration of influenza illness and can reduce the risk of influenza-related complications, including severe illness and death.
- Most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment or prophylaxis.
- However, persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age.
- Treatment with oseltamivir or zanamivir is recommended for all persons with suspected or confirmed influenza requiring hospitalization.
- Early empiric treatment with oseltamivir or zanamivir should be considered for persons with suspected or confirmed influenza who are at higher risk for complications including:
  - Children younger than 2 years old;
  - Persons aged 65 years or older;
  - Pregnant women and women up to 2 weeks postpartum (including following pregnancy loss);
  - Persons of any age with certain chronic medical or immunosuppressive conditions
    - ✓ Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological (including sickle cell disease), or metabolic disorders (including diabetes mellitus);
    - ✓ Disorders that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders)
    - ✓ Immunosuppression, including that caused by medications or by HIV; and
  - Persons younger than 19 years of age who are receiving long-term aspirin therapy.
- Children 2 years to 4 years old are more likely to require hospitalization or urgent medical evaluation for influenza compared with older children and adults, although the risk is much lower than for children younger than 2 years old. Children aged 2 years to 4 years without high risk conditions and with mild illness do not necessarily require antiviral treatment. [For more information on antiviral treatment of children and adolescents, see the supplementary guidance available at http://www.cdc.gov/h1n1flu/recommendations_pediatric_supplement.htm.]
- Treatment, when indicated, should be initiated as early as possible because the benefits are greatest when started within the first 2 days of illness. However, some studies of hospitalized patients with seasonal and 2009 H1N1 influenza have suggested benefit of antiviral treatment even when treatment was started more than 48 hours after illness onset.
- To reduce delays in treatment initiation, consider:

    - Informing persons at higher risk for influenza complications of signs and symptoms of influenza and need for early treatment after onset of symptoms of influenza (i.e., fever, respiratory symptoms);
    - Ensuring rapid access to telephone consultation and clinical evaluation for these patients as well as patients who report severe illness;
    - Considering empiric treatment of patients at higher risk for influenza complications based on telephone contact if hospitalization is not indicated and if this will substantially reduce delay before treatment is initiated.
- Treatment should not wait for laboratory confirmation of influenza because lab testing can delay treatment and because a negative rapid test for influenza does not rule out influenza. The sensitivity of rapid tests in detecting 2009 H1N1 has ranged from 10% to 70%. Information on the use of rapid influenza diagnostic tests (RIDTs) is found at http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm.
- Testing for 2009 H1N1 influenza infection with real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) should be prioritized for persons with suspected or confirmed influenza requiring hospitalization and based on guidelines from local and state health departments. [See page 3 of the Missouri Department of Health and Senior Services (DHSS) Health Update found at http://www.dhss.mo.gov/BT_Response/HAds/HU10SwineFlu9-11-09.pdf.]

Chemoprophylaxis

- Consideration for antiviral chemoprophylaxis should generally be reserved for persons at higher risk for influenza-related complications who have had close contact with someone likely to have been infected with influenza.
- However, early treatment is an emphasized alternative to chemoprophylaxis after a suspected exposure. Household or close contacts (with risk factors for influenza complications) of confirmed or suspected cases can be counseled about the early signs and symptoms of influenza, and advised to immediately contact their healthcare provider for evaluation and possible early treatment if clinical signs or symptoms develop. Early recognition of illness and treatment when indicated is preferred to chemoprophylaxis for vaccinated persons after a suspected exposure.
- Antiviral agents should not be used for post exposure chemoprophylaxis in healthy children or adults based on potential exposures in the community, school, camp, or other settings.
- For antiviral chemoprophylaxis of 2009 H1N1 influenza virus infection, either oseltamivir or zanamivir is recommended. Duration of post-exposure chemoprophylaxis is 10 days after the last known exposure to 2009 H1N1 influenza.
- Oseltamivir was authorized for use for chemoprophylaxis under the EUA for children younger than 1 year of age, subject to the terms and conditions of the EUA.
- [For important additional information on antiviral prophylaxis of children and adolescents, see the supplementary guidance at http://www.cdc.gov/h1n1flu/recommendations_pediatric_supplement.htm. Included in this guidance is the statement that oseltamivir chemoprophylaxis for influenza virus infection in children younger than 1 year old is age-based; however, chemoprophylaxis for asymptomatic infants less than 3 months old is not recommended due to lack of safety data.]
- Chemoprophylaxis generally is not recommended if more than 48 hours have elapsed since the last contact with an infectious person.
- Chemoprophylaxis is not indicated when contact occurred before or after, but not during, the ill person's infectious period.
- For these recommendations, the infectious period for influenza is defined as one day before illness onset until 24 hours after fever ends [without the use of fever reducing medications].

- Close contact, for the purposes of this document, is defined as having cared for or lived with a person who is a confirmed, probable, or suspected case of influenza, or having been in a setting where there was a high likelihood of contact with respiratory droplets and/or body fluids of such a person. Examples of close contact include sharing eating or drinking utensils, physical examination, or any other contact between persons likely to result in exposure to respiratory droplets. Close contact typically does not include activities such as walking by an infected person or sitting across from a symptomatic patient in a waiting room or office.

Additional Information

- Based on global experience to date, 2009 H1N1 influenza viruses likely will be the most common influenza viruses among those circulating in the coming season, particularly those causing influenza among younger age groups. Circulation of seasonal influenza viruses during the 2009-10 season is also expected. Influenza seasons are unpredictable, however, and the timing and intensity of seasonal influenza virus activity versus 2009 H1N1 circulation cannot be predicted in advance.
- Currently circulating 2009 H1N1 viruses are susceptible to oseltamivir and zanamivir, but resistant to amantadine and rimantadine; however, antiviral treatment regimens might change according to new antiviral resistance or viral surveillance information.
- Information on the dose and dosing schedule for oseltamivir and zanamivir is provided in the document (http://www.cdc.gov/h1n1flu/recommendations.htm). An April 2009 Emergency Use Authorization authorizes the emergency use of oseltamivir in children younger than 1 year old (http://www.cdc.gov/h1n1flu/eua/) subject to the terms and conditions of the EUA.

Note that this CDC guidance should be considered interim, and will be updated as needed. The current version will be available at http://www.cdc.gov/h1n1flu/recommendations.htm.

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Health Update:

2009 H1N1 Influenza Update 13: Antiviral Treatment of Hospitalized Patients, Peramivir EUA, New CDC Clinical Support Line, Reporting Selected Categories of Influenza Patients, Influenza Vaccinations and Pregnant Women

October 29, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov.

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

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Health Update
October 29, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 13: Antiviral Treatment of Hospitalized Patients, Peramivir EUA, New CDC Clinical Support Line, Reporting Selected Categories of Influenza Patients, Influenza Vaccinations and Pregnant Women**

This Health Update provides information on: 1) antiviral treatment options for hospitalized influenza patients; 2) Emergency Use Authorization (EUA) of peramivir; 3) a new CDC clinical support line for medical providers caring for pregnant/postpartum women; 4) reporting selected categories of influenza patients; 5) influenza vaccinations and pregnant women.

Antiviral Treatment Options for Hospitalized Patients with Suspected or Confirmed Influenza

The Centers for Disease Control and Prevention (CDC) has issued updated antiviral treatment options for hospitalized influenza patients utilizing the neuraminidase inhibitors (NAIs) oseltamivir, zanamivir, and peramivir. (The Food and Drug Administration [FDA] has recently issued an Emergency Use Authorization [EUA] to allow the use of peramivir to treat certain adult and pediatric patients with suspected or confirmed 2009 H1N1 influenza. See the next section for additional information on peramivir and the EUA.) The updated antiviral treatment options for hospitalized patients are available from CDC at http://www.cdc.gov/H1N1flu/EUA/peramivir_recommendations.htm. Key points include the following:

- Early treatment with oseltamivir has been associated with survival in hospitalized and critically ill patients with 2009 H1N1 influenza virus infection.
- Empiric antiviral treatment with oral oseltamivir or orally inhaled zanamivir should be administered as soon as possible for all persons with suspected or confirmed influenza requiring hospitalization. Initiation of antiviral treatment should not be delayed pending laboratory confirmation of influenza.
- Intravenous (IV) peramivir has been authorized for use by FDA, subject to the EUA terms and conditions.
- IV peramivir may be appropriate for certain hospitalized and critically ill patients with suspected or confirmed 2009 H1N1 influenza, such as patients not responding to either an oral or inhaled antiviral therapy and patients without a dependable oral or inhaled route of drug delivery (e.g. patients unable or unlikely to absorb oseltamivir due to ileus or high nasogastric tube output).
- Clinicians should carefully review the health care provider fact sheet on peramivir, (http://www.cdc.gov/h1n1flu/eua/Final%20HCP%20Fact%20sheet%20Peramivir%20IV_CDC.pdf). This fact sheet also includes the terms and conditions of the EUA, and safety and efficacy data on peramivir.
- To request IV peramivir (licensed clinicians with prescribing privileges ONLY), go to http://emergency.cdc.gov/h1n1antivirals/. For any questions, call 1-800-CDC-INFO (1-800-232-4636), 24 hours a day, 7 days a week.

Emergency Use Authorization (EUA) of Peramivir

Currently there are no FDA-approved IV antiviral products for the treatment of hospitalized patients with influenza. Peramivir is an investigational NAI available in IV formulation, whose efficacy and safety have not yet been established. FDA has recently issued an EUA to allow the use of peramivir to treat certain adult and pediatric patients with suspected or laboratory-confirmed 2009 H1N1 influenza. The following provides brief summary information on the use of peramivir under the EUA. For more comprehensive information, go to http://www.cdc.gov/h1n1flu/eua/peramivir.htm.

Peramivir is authorized for the following patients who are admitted to a hospital:

- Adult patients for whom therapy with an IV agent is clinically appropriate, based upon one or more of the following reasons:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible, or
  - the clinician judges IV therapy is appropriate due to other circumstances
- Pediatric patients for whom an IV agent is clinically appropriate because:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible

Do not use IV peramivir for the treatment of seasonal influenza A or B virus infections, for outpatients with acute uncomplicated 2009 H1N1 virus infection, or for pre- or post-exposure chemoprophylaxis (prevention) of influenza.

Clinical judgment is an important factor in determining which hospitalized or critically ill patients would benefit from IV peramivir. If peramivir is ordered, hospitalized patients should continue to receive therapy with an available NAI (oseltamivir or zanamivir) until after the first dose of peramivir has been administered. Combined therapy with oseltamivir or zanamivir and peramivir is not recommended because of their overlapping mechanism of action.

The standard adult dose of peramivir is 600 mg once a day, administered IV for 5 to 10 days. The decision to administer peramivir treatment longer than 5 days should be based upon clinical judgment and virological data (rRT-PCR or viral culture), if available.

Commonly reported adverse events in peramivir clinical trials were diarrhea, nausea, vomiting, and neutropenia. Additional adverse events associated with the drug, some of which may be serious, may become apparent with more widespread use.

Clinicians considering the use of peramivir under the EUA must read and understand the content of the provider fact sheet (http://www.cdc.gov/h1n1flu/eua/Final%20HCP%20Fact%20sheet%20Peramivir%20IV_CDC.pdf) and the terms and conditions on the EUA prior to initiating a request for this product. The fact sheet also contains the limited available safety and efficacy data, as well as dosing information, including the recommended dose with renal insufficiency.

If medical providers, after reviewing materials available at http://www.cdc.gov/h1n1flu/eua/peramivir.htm, have clinical questions relating to the use of IV peramivir, they should contact CDC INFO at 1-800-232-4636, 24 hours a day, 7 days a week. (For TTY, call 1-888-232-6348.)

To request IV peramivir, clinicians should go to http://emergency.cdc.gov/h1n1antivirals/.

(Clinicians interested in enrolling patients in clinical trials of IV antiviral agents for influenza should contact the investigators of pertinent clinical trials [http://clinicaltrials.gov/].)

(Note on IV zanamivir: IV zanamivir is available for compassionate use from its manufacturer via an emergency Investigational New Drug (IND) application to FDA. Go to FDA's IND Application Web site at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm.)

CDC Clinical Support Line for Medical Providers Caring for Pregnant/Postpartum Women

CDC has established a new clinical support line to provide technical assistance to medical providers caring for seriously ill pregnant or immediately postpartum (within 6 weeks of delivery) women with influenza. The telephone number is 404-368-2133. Clinical support is available from board-certified OB/GYN subject matter experts 24 hours a day, 7 days a week. Note that this number should only be used for consultation on seriously ill pregnant or postpartum patients, or to report seriously ill pregnant or immediately postpartum patients who are admitted to an intensive care unit (ICU) or who die (see the next section). For questions regarding pregnant women who are not seriously ill, providers can call 1-800-232-4636.

Reporting Selected Categories of Influenza Patients

The following influenza cases should be reported directly to CDC:

1. Any pregnant or immediately postpartum (within 6 weeks of delivery) woman with severe influenza (2009 H1N1 or seasonal) who is either: a) admitted to an ICU, or b) dies. The report should be made by calling 404-368-2133, or by completing the case report form available at http://www.dhss.mo.gov/BT_Response/SwineFlu/PregnantandPostPartumWomen.pdf and faxing it to 404-248-4094.

2. Any patient with 2009 H1N1 influenza virus infection suspected of having hemorrhagic pneumonitis syndrome (HPS). Suspected HPS can be considered in a patient with all of the following:
   - Confirmed 2009 H1N1 virus infection, and
   - Clinical or radiographic evidence of pneumonia, and
   - Acute onset of illness accompanied by dyspnea and hemoptysis, and
   - Severe respiratory illness requiring mechanical ventilation or resulting in death

   OR
   - Confirmed H1N1 virus infection, and
   - A bronchoalveolar lavage (BAL) specimen with hemorrhagic fluid, or hemosiderin laden macrophages on Prussian blue staining

   The report should be made by completing the HPS case report form, which is available at http://www.dhss.mo.gov/BT_Response/SwineFlu/HPS.pdf, and faxing pages 2-7 to 404-639-3866 (ATTN: Erin Kennedy).

All influenza-associated pediatric deaths (≤18 years of age) should be reported within one day to the local public health agency, or to the Missouri Department of Health and Senior Services (DHSS) at 573-751-6113 or 800-392-0272. For all suspected or confirmed influenza-associated pediatric deaths, a DHSS disease case report (CD-1) form (http://www.dhss.mo.gov/CommunicableDisease/CD-1.pdf) should be completed. In addition, for all confirmed influenza-associated pediatric deaths, a separate CDC influenza-associated pediatric death report form (http://www.dhss.mo.gov/CDManual/PedDeathform.pdf) should also be completed.

Influenza Vaccinations and Pregnant Women

The following is from an October 22, 2009, press release from the American Medical Association (AMA), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG).

To help stress the urgent message that pregnant women must get vaccinated against both seasonal influenza and 2009 H1N1 to protect themselves and their unborn baby, the AMA, AAFP, ACOG, and CDC joined forces today. In a group letter sent to health care professionals nationwide, leaders from the four groups emphasized the increased number of deaths among pregnant women from influenza and provided helpful information for medical professionals.

The letter urges health care professionals to vaccinate their pregnant patients and counsel them on the benefits of the vaccine. Both the seasonal influenza vaccine and the H1N1 vaccine are safe to administer to pregnant women in any trimester and can be given simultaneously. Pregnant women should be given the flu shot, not the nasal spray version of the vaccine.

[See the letter at http://www.acog.org/departments/resourceCenter/2009H1N1JointDearColleagueLtr.pdf.]

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html.

Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).

Health Update:

2009 H1N1 Influenza Update 14: Antiviral Drugs from the SNS, Key Issues Concerning Antivirals, Peramivir Availability, H1N1 Vaccines, Clinical Support Line for Providers of Care to Pregnant/Postpartum Women

November 13, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov.

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

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Health Update
November 13, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 14: Antiviral Drugs from the SNS, Key Issues Concerning Antivirals, Peramivir Availability, H1N1 Vaccines, Clinical Support Line for Providers of Care to Pregnant/Postpartum Women**

This Health Update provides information on: 1) antiviral medications from the SNS; 2) key issues concerning antivirals; 3) availability of peramivir; 4) 2009 H1N1 influenza vaccines; 5) CDC clinical support line for medical providers caring for pregnant/postpartum women.

Antiviral Medications from the Strategic National Stockpile (SNS)

Missouri has received antiviral medications from the Strategic National Stockpile (SNS): Tamiflu 30 mg, 45 mg, and 75 mg capsules; Tamiflu oral suspension; and Relenza inhalation powder. These medications are intended for treatment of persons with known or suspected influenza, and should only be utilized when all local resources have been exhausted. Exhausted local resources may include the unavailability of the drug in area pharmacies and hospitals, and also the patient's inability to pay for the drug. Antivirals obtained from the SNS cannot be used for chemoprophylaxis.

Most of the antiviral medications received from the SNS have been transferred to local public health agencies (LPHAs) throughout the state. Each LPHA has developed antiviral dispensing plans, and identified community partners to dispense these drugs. These plans include written agreements with physicians, pharmacies, hospitals, and other healthcare facilities which dispense medication. Plans may vary by jurisdiction depending on the availability of healthcare resources, and the partnerships that have been developed with dispensers. For a listing of community partners who are dispensing SNS antiviral medications, contact your LPHA. A listing of these agencies can be found at: http://www.dhss.mo.gov/LPHA/LPHAs.html.

Key Issues for Clinicians Concerning Antiviral Treatments

The Centers for Disease Control and Prevention (CDC) has stated that most healthy persons who develop an illness consistent with uncomplicated influenza, or persons who appear to be recovering from influenza, do not need antiviral medications for treatment. However, for some individuals antiviral treatment is recommended. (See the current CDC antiviral guidance at http://www.cdc.gov/h1n1flu/recommendations.htm. See also information on antiviral safety at http://www.cdc.gov/H1N1flu/antivirals/safety_info.htm)

CDC has found that among ill persons who would be recommended to receive antiviral treatment, not all are being treated. To help address this situation, CDC has recently issued a document entitled "Key Issues for Clinicians Concerning Antiviral Treatments for 2009 H1N1" (http://www.cdc.gov/H1N1flu/HAN/110609.htm), whose content is reproduced here:

> *Although use of influenza antiviral drugs in the United States has increased during the 2009-2010 flu season, not all people recommended for antiviral treatment are getting treated. Listed below are important facts to consider when deciding whether a patient needs to be treated with antiviral medication.*
>
> ***It is critical to remember that it is not too late to treat, even if symptoms began more than 48 hours ago.*** *Although antiviral treatment is most effective when begun within 48 hours of influenza illness onset, studies have shown that hospitalized patients still benefit when treatment with oseltamivir is started more than 48 hours after illness onset.* ***Outpatients, particularly those with risk factors for severe illness who are***

***not improving, might also benefit from treatment initiated more than 48 hours after illness onset*.**

Recommendations for Clinicians

Many 2009 H1N1 patients can benefit from antiviral treatment, and **all hospitalized patients with suspected or confirmed 2009 H1N1 should receive antiviral treatment with a neuraminidase inhibitor – either oseltamivir or zanamivir – as early as possible** after illness onset. Moderately ill patients, especially those with risk factors for severe illness, and those who appear to be getting worse, can also benefit from treatment with neuraminidase inhibitors. A full listing of risk factors for severe influenza is available at: http://www.cdc.gov/h1n1flu/highrisk.htm.

Although antiviral medications are recommended for treatment of 2009 H1N1 in patients with risk factors for severe disease, **some people without risk factors may also benefit from antivirals**. To date, 40% of children and 20% of adults hospitalized with complications of 2009 H1N1 did not have risk factors. Clinical judgment is always an essential part of treatment decisions.

When treatment of persons with suspected 2009 H1N1 influenza is indicated, it **should be started empirically. If a decision is made to test for influenza, treatment should not be delayed while waiting for laboratory confirmation**. The earlier antiviral treatment is given, the more effective it is for the patient. Also, rapid influenza tests often can give false negative results. If you suspect flu and feel antiviral treatment is warranted, treat even if the results of a rapid test are negative. Obtaining more accurate testing results can take more than one day, so treatment should not be delayed while waiting for these test results. For more information on influenza testing, please see: http://www.cdc.gov/h1n1flu/guidance/diagnostic_tests.htm.

Although commercially produced pediatric oseltamivir suspension is in short supply, **there are ample supplies of children's oseltamivir capsules, which can be mixed with syrup at home. In addition, pharmacies can compound adult oseltamivir capsules into a suspension for treatment of ill infants and children.** Additional information on compounding can be found at: http://www.cdc.gov/H1N1flu/pharmacist/.

For More Information

Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season: http://www.cdc.gov/H1N1flu/recommendations.htm.

Questions & Answers: Antiviral Drugs, 2009-2010 Flu Season: http://www.cdc.gov/h1n1flu/antiviral.htm.

Influenza Diagnostic Testing: http://www.cdc.gov/h1n1flu/diagnostic_testing_clinicians_qa.htm.

Updated Interim Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season: http://www.cdc.gov/H1N1flu/pregnancy/antiviral_messages.htm.

Antiviral Drugs: Summary of Side Effects: http://www.cdc.gov/flu/protect/antiviral/sideeffects.htm.

General information for the public on antiviral drugs is available in "2009 H1N1 and Seasonal Flu: What You Should Know About Flu Antiviral Drugs" at http://www.cdc.gov/H1N1flu/antivirals/geninfo.htm.

Downloadable brochures and informational flyers, including one on antiviral drugs, are available at http://www.cdc.gov/h1n1flu/flyers.htm.

For the FDA page on antiviral influenza drugs: http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm.

For additional information, you can also call CDC's toll-free hotline, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, which is available 24 hours a day, every day.

Availability of Intravenous Peramivir

The Food and Drug Administration (FDA) has recently issued an Emergency Use Authorization (EUA) to allow use of the neuraminidase inhibitor peramivir for the treatment of certain hospitalized patients with known or suspected 2009 H1N1 influenza. For more information on peramivir, see http://www.cdc.gov/h1n1flu/eua/peramivir.htm and http://www.cdc.gov/h1n1flu/EUA/pdf/peramivir_qa.pdf.

Peramivir can be requested through CDC by going to http://emergency.cdc.gov/h1n1antivirals/. Note that as part of this request, the clinician must acknowledge his/her compliance with the terms and conditions of the EUA.

Information on 2009 H1N1 Influenza Vaccines

Supplies of 2009 H1N1 vaccines are now coming into Missouri, and more will become available in the coming weeks. See http://www.dhss.mo.gov/BT_Response/_provider_listing.html for current information on 2009 H1N1 and seasonal influenza vaccines in the state. Knowing that initial supplies of 2009 H1N1 vaccines would be limited, the Advisory Committee on Immunization Practices (ACIP) has recommended that vaccination efforts first be directed to certain priority groups (see http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5810a1.htm). Contact your LPHA for recommendations on how vaccine is being distributed in your area.

The following are sources of information for clinicians on 2009 H1N1 influenza vaccines:

- DHSS Issues Exemption for 2009 H1N1 Influenza Vaccine (DHSS)
  http://www.dhss.mo.gov/NewsAndPublicNotices/2009/h1n1vaccinewaiver.html

  The Missouri Department of Health and Senior Services (DHSS) recently issued an exemption (which applies only to 2009 H1N1 influenza vaccine) that temporarily sets aside a statute which prohibited pregnant women and children under three from receiving vaccine containing thimerosal.

- Update on Influenza A (H1N1) 2009 Monovalent Vaccines (CDC)
  http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5839a3.htm

- Monovalent Influenza Vaccine Dosage, Administration, and Storage (CDC)
  http://www.cdc.gov/h1n1flu/vaccination/dosage.htm

- Influenza A (H1N1) 2009 Monovalent (FDA)
  http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm181950.htm

  Includes links to the package insert for each of the licensed vaccines.

- Vaccine Information Statements: 2009 H1N1 Influenza Vaccines (CDC)
  http://www.cdc.gov/vaccines/pubs/vis/default.htm#h1n1live

- Model Standing Orders for Administering 2009 H1N1 Vaccine and for Treatment of Post-Vaccination Reactions (DHSS)
  http://www.dhss.mo.gov/BT_Response/model_standing_orders.pdf

CDC has developed several sets of questions and answers on 2009 H1N1 influenza vaccines. A selection of these questions and answers, arranged by category, is found in the Appendix beginning on the next page.

CDC Clinical Support Line for Medical Providers Caring for Pregnant/Postpartum Women

As mentioned in Health Update 13, CDC has established a new clinical support line to provide technical assistance to medical providers caring for seriously ill pregnant or immediately postpartum (within 6 weeks of delivery) women with influenza. The telephone number is 404-368-2133. Clinical support is available from board-certified OB/GYN subject matter experts 24 hours a day, 7 days a week. Note that this number should only be used for consultation on seriously ill pregnant or postpartum patients, or to report seriously ill pregnant or immediately postpartum patients who are admitted to an intensive care unit (ICU) or who die (see Health Update 12). For questions regarding pregnant women who are not seriously ill, providers can call 1-800-232-4636.

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html. Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).

APPENDIX
Questions and Answers on 2009 H1N1 Influenza Vaccines

The following questions and answers on the 2009 H1N1 influenza vaccines are from materials prepared by the Centers for Disease Control and Prevention (CDC), and are arranged in the following categories:

2009 H1N1 Live Attenuated (LAIV) Vaccine

See also the section below entitled "Simultaneous and Sequential Administration of 2009 H1N1 Vaccines and Other Vaccines"

Can the nasal-spray flu vaccine be used together with influenza antiviral medications?

If a person is taking an influenza antiviral drug (including Tamiflu® or Relenza®, then the nasal spray flu vaccine should not be given until 48 hours after the last dose of the influenza antiviral medication was given.

If a person takes antiviral drugs within two weeks of getting the nasal spray flu vaccine, that person should get revaccinated. (The antiviral drugs will have killed the vaccine viruses that are supposed to cause the immune response against those viruses.)

Antiviral drugs can be taken with the inactivated (i.e. killed) flu vaccine.[1]

Can people receiving the nasal-spray flu vaccine LAIV pass the vaccine viruses to others?

In clinical studies, transmission of vaccine viruses to close contacts occurred only rarely. The current estimated risk of getting infected with vaccine virus after close contact with a person vaccinated with the nasal-spray flu vaccine is low (0.6%-2.4%). Because the viruses are weakened, infection is unlikely to result in influenza illness symptoms since the vaccine viruses have not been shown to change into typical or naturally occurring influenza viruses.[1]

Can contacts of people with weakened immune systems get the nasal-spray flu vaccine?

People who are in contact with others with severely weakened immune systems when they are being cared for in a protective environment (for example, people with hematopoietic stem cell transplants), should not get the nasal spray vaccine, including the 2009 H1N1 nasal spray vaccine if they will come into contact with the severely immunocompromised person within 7 days of vaccination. People who have contact with others with lesser degrees of immunosuppression (for example, people with diabetes, people with asthma taking corticosteroids, or people infected with HIV) can get the nasal spray vaccine.[1]

Can a person who has received LAIV test positive on a rapid influenza diagnostic test?

The live attenuated influenza vaccine viruses in LAIV (seasonal vaccine and 2009 H1N1 monovalent vaccine) can cause a positive result on a rapid influenza diagnostic test. The tests are designed to detect influenza viruses and cannot differentiate between live attenuated and wild-type influenza viruses. A positive test in a person who recently (in the previous 7 days) received LAIV and who also has an influenza-like illness could be caused by either LAIV or wild-type influenza virus.[2]

Can health care providers get the live attenuated influenza vaccine?

Yes. LAIV is a very good option for most health care providers who are healthy, younger than 50 years old, and not pregnant. However, health care providers should not get LAIV if they are providing medical care for patients who require special environments in the hospital because they are profoundly immunocompromised (e.g., those who work in bone marrow transplant units). Although no immunocompromised patient has been shown to be harmed by use of LAIV among health care workers, the recommendation against the use of LAIV in health care workers with this type of patient contact is intended as an extra precaution for fragile immunocompromised patients. Health care workers with this type of patient contact can get LAIV, but if they do, they should wait 7 days after being vaccinated before returning to duties that include care of severely immunocompromised patients in special environments.[1]

Can health care personnel in a neonatal intensive care unit (NICU) get LAIV?

Yes. Either the inactivated injectable influenza vaccine or the LAIV can be given to health care personnel working in a neonatal intensive care unit (NICU). Nearly all healthy, non-pregnant health care workers, including those who come in contact with newborn infants, pregnant women, persons with a solid organ transplant, persons receiving chemotherapy (not in preparation for a bone marrow transplant), and persons with HIV/AIDS, may receive LAIV if otherwise eligible. However, LAIV should not be

used for health care personnel who care for patients undergoing bone marrow transplantation (i.e., patients who require a protected environment).

No special precautions (e.g., masks or gloves) are necessary for health care personnel who have been vaccinated with the LAIV and who do not work with patients undergoing bone marrow transplantation. However, for health care personnel that were vaccinated with LAIV and who work with patients undergoing bone marrow transplantation, the ACIP recommends, as a precautionary measure, that those health care personnel avoid providing care for such patients for 7 days after vaccination.[1]

Can health care workers who cannot receive the nasal spray vaccine (e.g., pregnant women, older adults, persons with chronic medical conditions) administer this vaccine to others?
Yes. Health care workers who cannot get the nasal spray vaccine themselves can administer the vaccine to others.[1]

What personal protective equipment is recommended for health care workers who are giving the 2009 H1N1 nasal spray vaccine?
Personal protective equipment (gloves and masks) are not needed when administering the nasal spray vaccine, including the 2009 H1N1 nasal spray vaccine.[1]

Use of 2009 H1N1 Vaccine in Children 6 Months Through 9 Years of Age

Children ages 6 months through 8 years receiving seasonal influenza vaccination for the first time are recommended to receive 2 doses. However, in the prescribing information (package inserts) for 2009 H1N1 monovalent influenza vaccines, children ages 6 months through 9 years are recommended to receive 2 doses. Does CDC recommend that clinicians follow the recommendation in the 2009 H1N1 monovalent vaccine package inserts or use the standard seasonal vaccine recommendations?
The recommendations for use of seasonal vaccine are unchanged – children 6 months through 8 years receiving seasonal influenza for the first time are recommended to receive 2 doses. Other children just need one dose of seasonal influenza vaccine.

Using the 2009 H1N1 monovalent influenza vaccine schedule presented in the prescribing information is recommended (6 months through 9 years receive 2 doses regardless of earlier vaccination with seasonal influenza vaccine).[3]

The interval between doses stated in the 2009 H1N1 monovalent influenza vaccine prescribing information is "approximately 1 month". What does "approximately 1 month" mean?
CDC recommends that the two doses of 2009 H1N1 monovalent vaccines be separated by 28 days (4 weeks).[3]

The 2009 H1N1 monovalent influenza vaccine trials that are currently underway have often used a 21 day (3 week) interval between doses. Is a 21 day interval acceptable for inactivated 2009 H1N1 monovalent vaccines?
CDC recommends that the two doses of 2009 H1N1 monovalent influenza vaccines be separated by 28 or more days (4 weeks). However, trials of the inactivated 2009 H1N1 vaccines have often used a 21 day interval. Administering the two doses of a 2009 H1N1 monovalent inactivated influenza vaccine at least 21 days apart is safe and acceptable. Therefore, if the second dose of an inactivated 2009 H1N1 monovalent vaccine is separated from the first dose by at least 21 days, the second dose can be considered valid. If the interval separating the doses is less than 21 days, the second dose should be repeated 28 or more days after the invalid (second) dose ($\geq$ 21 days is acceptable for this interval also).[3]

Can a child who requires 2 doses of a 2009 H1N1 monovalent influenza vaccine and who received the first dose with an inactivated 2009 H1N1 monovalent vaccine complete the series with the 2009 H1N1 monovalent LAIV, or vice versa?
There are limited data describing the immune response to mixed schedules. Therefore, when feasible, the same type of vaccine (live attenuated or inactivated) should be used in a two-dose schedule. Mixed schedules however, are preferable to not completing the series. A 28 day interval between doses is recommended, but 21 days is acceptable. If vaccines are separated by 1-20 days, repeat the invalid (second) dose 28 days (21 days acceptable) from the invalid second dose.[3]

Pregnant Women

How many vaccine doses will a pregnant woman need to get?
The U.S. Food and Drug Administration (FDA) has approved the use of one dose of vaccine for full protection for persons 10 years and older. Therefore, a pregnant woman is recommended to get one dose of the 2009 H1N1 monovalent vaccine.[2]

Can the 2009 H1N1 monovalent flu vaccine be given at any time during pregnancy?
Seasonal flu vaccine is recommended for all pregnant women at any time during pregnancy, and has not been shown to cause harm to a pregnant woman or her baby. The Advisory Committee on Immunization Practices also recommends that 2009 H1N1 monovalent flu vaccine be given to all pregnant women at any time during pregnancy.[4]

Can pregnant women receive the nasal spray vaccine?
The nasal spray vaccine is not licensed for use by pregnant

women. Pregnant women should not receive nasal spray vaccine for either seasonal flu or 2009 H1N1 flu. After delivery, women can receive the nasal spray vaccine, even if they are breastfeeding.[4]

What if a pregnant woman receives the live attenuated influenza vaccine?

Live attenuated influenza vaccines (seasonal or H1N1 LAIV) have not been studied in pregnant women and LAIV is not recommended for pregnant women. The inactivated influenza vaccines (seasonal and 2009 monovalent H1N1) are recommended for pregnant women. However, if a pregnant woman receives LAIV, for example, before she knows she is pregnant, she would not be expected to have any additional risks, compared with women who are not pregnant. The influenza vaccine virus replicates in the nose where body temperature is lower and has never been shown to replicate in other parts of the body or be passed to the unborn baby.

There are not any special measures to be taken if a pregnant woman has received live vaccine, i.e., revaccination with inactivated vaccine, taking antivirals, or enhanced testing. She should have pregnancy monitoring and testing as clinically indicated.

CDC and FDA are requesting that these instances of using LAIV in pregnant women be reported to the Vaccine Adverse Event Reporting System (VAERS). This will allow us to track these instances, even if there is no adverse event following the incident.[4]

For planned pregnancies, how long should a woman wait after receiving nasal spray flu vaccines before becoming pregnant?

There are no studies of live attenuated influenza vaccine among women who are pregnant or who are planning to become pregnant. However, the vaccine virus is cold-adapted and replicates in the nasopharyngeal tissues rather than at core body temperature. Consequently, infection of a fetus with live attenuated influenza virus is very unlikely. It is not necessary to defer pregnancy for a specific interval following receipt of live attenuated influenza vaccine.[2]

Can pregnant women be in contact with someone who has gotten the nasal spray vaccine (LAIV)?

Yes. A pregnant woman can be in close contact with someone who has gotten the nasal spray flu vaccine (LAIV). A pregnant woman can also administer (give) a nasal spray vaccine (LAIV). Because the viruses in the nasal spray vaccine are attenuated or weakened, vaccine viruses are unlikely to cause any illness symptoms, even if an unvaccinated person inadvertently gets vaccine viruses in their nose. The nasal spray vaccine against seasonal influenza viruses has been used in millions of school children and healthy adults since it was licensed, and there have been no reports of pregnant women becoming ill after exposure to their vaccinated children or other family members.

While it's OK for her contacts to get the nasal spray vaccine, this vaccine should not be given to pregnant women. While LAIV is not known to be a safety risk for pregnant women, there have not been studies of LAIV among pregnant women to assess safety and effectiveness for use in this group. LAIV can be given to women after they have delivered, even if they are nursing.

CDC recommends that pregnant women get both the 2009 H1N1 flu shot and the seasonal flu shot. Flu shots are made with a killed virus, and have not been shown to cause harm to pregnant women or their babies.[1]

If a pregnant woman delivers her baby before receiving her seasonal flu shot or her 2009 H1N1 flu shot, should she still receive them?

Yes. In addition to protecting her from infection, the vaccine may also help protect her young infant. Flu vaccines are recommended only for infants 6 months or older. It is recommended that everyone who lives with or provides care for an infant less than 6 months old receive both the seasonal flu vaccine and the 2009 H1N1 monovalent flu vaccine.[4]

Can a woman who is breastfeeding receive the vaccine?

Yes. Both seasonal flu and 2009 H1N1 monovalent influenza vaccines should be given to breastfeeding mothers. Breastfeeding is fully compatible with flu vaccination, and preventing maternal infection provides secondary protection to the infant. Maternal vaccination is especially important for infants less than 6 months old, who are ineligible for vaccination. In addition, transfer of vaccination-related antibodies by breastfeeding further reduces the infant's chances of getting sick with the flu. While pregnant women should just receive the inactivated injectable form of influenza vaccine, nursing mothers can receive either the injectable or nasal spray form.[4]

Is the 2009 H1N1 monovalent flu vaccine safe for pregnant women?

Flu vaccines have not been shown to cause harm to a pregnant woman or her baby. The seasonal flu shot has been recommended for pregnant women for many years. The 2009 H1N1 monovalent flu vaccine will be made using the same processes as the seasonal flu vaccine, and clinical trials of H1N1 monovalent vaccine safety in non-pregnant children and adults found results similar to those seen in studies of seasonal flu vaccine. Studies that test the 2009 H1N1 monovalent flu vaccine in pregnant women began in September. For more information, see: http://www3.niaid.nih.gov/news/QA/vteuH1N1qa.htm.[4]

Does the 2009 H1N1 monovalent flu vaccine have preservative in it?

Multi-dose vials of flu vaccine contain the preservative thimerosal to prevent bacterial growth. There is no evidence that thimerosal is harmful to a pregnant woman or a fetus. However, because some women are concerned about exposure to preservatives during pregnancy, manufacturers are producing preservative-free seasonal flu vaccine and 2009 H1N1 monovalent flu vaccine in single dose syringes. CDC recommends that pregnant women receive flu vaccine with or without thimerosal.[4]

Does the 2009 H1N1 monovalent flu vaccine have an adjuvant or squalene in it?
Adjuvants are agents that are sometimes added to a vaccine to increase its effectiveness. There are no adjuvants (such as squalene) in either the 2009 H1N1 monovalent or seasonal flu vaccines used in the United States.[4]

Vaccinating Persons Who Have Had Influenza-Like Illness

Will the 2009 H1N1 vaccine be recommended for patients who had influenza-like illness since spring 2009?
All people in a recommended vaccination target group who did not have 2009 H1N1 virus infection confirmed by real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) test should be vaccinated with the 2009 H1N1 vaccine. People who had an illness confirmed by rRT-PCR to be 2009 H1N1 virus earlier in 2009 can be considered to be immune and do not need to be vaccinated this year. However, most people with respiratory illnesses since this spring have not had testing with the rRT-PCR test, which is the only test that can confirm infection specifically with the 2009 H1N1 virus. Tests such as rapid antigen detection assays and diagnoses based on symptoms alone without rRT-PCR testing, cannot specifically determine if a person has 2009 H1N1 influenza. Although people who were not tested, but who became ill within 1-4 days after close contact with a person with lab confirmed 2009 H1N1 influenza might have been infected with 2009 H1N1, they cannot be certain since many pathogens can cause respiratory illness. These people should get the 2009 H1N1 vaccine as recommended for their age and risk group.

People who were infected with the 2009 H1N1 virus and who are not severely immune compromised will likely have immunity to subsequent infection with 2009 H1N1 virus. However, vaccination of a person with some existing immunity to the 2009 H1N1 virus will not be harmful, and patients who are uncertain about how they were diagnosed should get the 2009 H1N1 vaccine. In addition, people recommended for seasonal vaccine should get a seasonal vaccine because infection with the 2009 H1N1 virus does not provide protection against seasonal influenza viruses.[2]

Simultaneous and Sequential Administration of 2009 H1N1 Vaccines and Other Vaccines

Can 2009 H1N1 vaccine be administered at the same visit as other vaccines?
Inactivated 2009 H1N1 vaccine can be administered at the same visit as any other vaccine, including pneumococcal polysaccharide vaccine. Live 2009 H1N1 vaccine can be administered at the same visit as any other live or inactivated vaccine **EXCEPT** seasonal live attenuated influenza vaccine.[2]

Can seasonal influenza vaccine and 2009 H1N1 vaccine be given at the same visit?
Both seasonal and 2009 H1N1 vaccines are available as inactivated and live attenuated (LAIV) formulations.

The simultaneous and sequential administration of seasonal and 2009 H1N1 inactivated vaccines is currently being studied. However, existing recommendations are that two inactivated vaccines can be administered at any time before, after, or at the same visit as each other (General Recommendations on Immunization, *MMWR* 2006;55[RR-15]).

Existing recommendations also state that an inactivated and live vaccine may be administered at any time before, after or at the same visit as each other. Consequently, providers can administer seasonal and 2009 H1N1 inactivated vaccines, seasonal inactivated vaccine and 2009 H1N1 LAIV, or seasonal LAIV and inactivated 2009 H1N1 at the same visit, or at any time before or after each other.

Live attenuated seasonal and live 2009 H1N1 vaccines should **NOT** be administered at the same visit until further studies are done.[2]

What is the minimum interval between doses of seasonal LAIV and 2009 H1N1 monovalent LAIV?
There are no data on sequential administration of seasonal and 2009 H1N1 monovalent LAIV. The ACIP recommends a minimum interval of 28 days (4 weeks) between use of a seasonal LAIV and a 2009 H1N1 monovalent LAIV because these are considered to be 2 different vaccines. The ACIP recommendations were developed based on data from studies using attenuated injectable live virus vaccines such as the measles, mumps and rubella vaccine. Trials of 2009 H1N1 live attenuated vaccines have used a 28 day interval between doses and therefore, 28 days is the recommended interval between 2 doses of LAIV (seasonal and H1N1 monovalent LAIV). However, based on previous studies of LAIV replication and immune response, as little as 14 days (2 weeks) might be sufficient to allow for an appropriate immune response to both vaccines. Therefore, an interval between the two types of LAIV of 2 weeks or more may be acceptable, although an interval

of 28 days is preferred.[3]

If seasonal LAIV and 2009 H1N1 monovalent LAIV are not administered on the same day, but are separated by less than 14 days (2 weeks), do either or both doses need to be repeated, and if so, when?
Seasonal LAIV and 2009 H1N1 monovalent LAIV should not be administered at the same visit, and should be separated by at least 28 days (14 days acceptable based on previous studies of attenuated influenza vaccine virus replication and immune response). If accidentally given at the same visit, neither dose needs to be repeated. If given 1-13 days apart, the second dose should be repeated 28 days (14 days acceptable) from the invalid (second) dose.[3]

If seasonal LAIV and 2009 H1N1 monovalent LAIV are inadvertently given at the same visit, do either or both doses need to be repeated, and if so, when?
Seasonal LAIV and 2009 H1N1 monovalent LAIV should not be administered at the same visit. While use of the 2 types of LAIV at the same visit could result in reduced immunogenicity for one vaccine, according to some experts, there are no data describing what happens with the vaccine response following simultaneous administration of LAIV vaccines. However, if both types of LAIV are inadvertently administered at the same visit neither vaccine, needs to be repeated.[3]

Adverse Reactions

What are the possible side effects of the 2009 H1N1 monovalent flu vaccine?
The side effects from 2009 H1N1 monovalent flu vaccine are expected to be similar to those from seasonal flu vaccines. The most common side effects following vaccination are expected to be mild, such as soreness, redness, tenderness, or swelling where the shot was given. Some people might experience headache, muscle aches, fever, fatigue, and nausea. If these problems occur, they usually begin soon after the shot is given and may last as long as 1-2 days. Fainting may occur shortly after receiving any injection and has uncommonly been reported after the flu shot. Like any medicines, vaccines can cause serious problems like severe allergic reactions. However, life-threatening allergic reactions to vaccines are very rare.

Pregnant women are not known to have an increased risk of side effects from the flu vaccine.

Anyone who has a severe (life-threatening) allergy to eggs or to any other substance in the vaccine should not get the vaccine. Providers should ask patients whether they have any severe allergies or if they have ever had a severe allergic reaction following flu vaccination.[4]

Is the 2009 H1N1 flu vaccine expected to be associated with Guillain-Barre Syndrome (GBS)?
During the 1976 Swine Flu vaccination program in the U.S., using a vaccine virus very different than the 2009 H1N1 virus, the 1976 vaccine was associated with cases of a severe paralytic illness called Guillain-Barre Syndrome (GBS). Approximately 1 additional case of GBS per 100,000 persons vaccinated occurred with the 1976 swine flu vaccine. Most studies done on seasonal flu vaccines after the 1976 vaccine showed no increased risk of GBS. However, two studies did demonstrate a small risk of approximately 1 additional case of GBS per 1 million persons vaccinated.

GBS occurs at a rate of 10-20 cases per 1 million adults, per year, regardless of vaccination. Substantial evidence exists that multiple infectious illnesses, most notably *Campylobacter jejuni* gastrointestinal infections and upper respiratory tract infections, including respiratory illness caused by influenza, are associated with GBS.

In general, seasonal flu vaccine has not been found to increase the risk for GBS. If a risk exists, it is low (i.e., approximately one additional case per 1 million persons vaccinated). The potential benefits of flu vaccination in preventing serious illness, hospitalization, and death substantially outweigh this estimate of risk for flu vaccine-associated GBS. Persons who have previously had GBS should not receive influenza vaccine.[4]

What can providers do if there is a clinical adverse event following vaccine administration?
The Vaccine Adverse Event Reporting System (VAERS) is a US vaccine safety surveillance system, co-managed by CDC and FDA.

Clinically significant adverse events that follow vaccination should be reported to VAERS. Reports may be filed securely online at http://vaers.hhs.gov/, by mail, or by fax. Report forms are available online or can be obtained by calling 1-800-822-7967 to request reporting forms or other assistance.[4]

Sources:

1. CDC. *Questions & Answers: 2009 H1N1 Nasal Spray Vaccine*, October 7, 2009. http://www.cdc.gov/h1n1flu/vaccination/nasalspray_qa.htm

2. CDC. *H1N1 Clinicians Questions and Answers*, October 23, 2009. http://www.cdc.gov/h1n1flu/vaccination/clinicians_qa.htm

3. CDC. *Frequently asked questions on use of influenza A(H1N1) 2009 monovalent vaccines (2009 H1N1 monovalent influenza vaccines): Practical considerations for immunization programs and providers*, November 10, 2009. http://www.cdc.gov/H1N1flu/vaccination/top10_faq.htm

4. CDC. *2009 H1N1 Influenza Vaccine and Pregnant Women: Information for Healthcare Providers*, November 2, 2009. http://www.cdc.gov/h1n1flu/vaccination/providers_qa.htm

Health Update:

2009 H1N1 Influenza Update 15: Management of Maternal Infection in Intrapartum and Postpartum Hospital Settings, Pneumococcal Vaccination Recommendations

November 19, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov.

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Health Update
November 19, 2009

FROM: **MARGARET T. DONNELLY**
DIRECTOR

SUBJECT: **2009 H1N1 Influenza Update 15: Management of Maternal Infection in Intrapartum and Postpartum Hospital Settings, Pneumococcal Vaccination Recommendations**

This Health Update provides information on: 1) management of maternal infection with 2009 H1N1 influenza virus in intrapartum and postpartum hospital settings; and 2) the use of pneumococcal vaccines to help prevent secondary pneumococcal infections following infection with influenza virus.

Management of Maternal Infection in Intrapartum and Postpartum Hospital Settings

The Centers for Disease Control and Prevention (CDC) has released updated guidance which clarifies clinical considerations related to management of suspected or confirmed maternal infection with 2009 H1N1 influenza virus infection within labor and delivery, postpartum, and newborn care settings in hospitals. The following provides a summary of the guidance. The complete document is found at: http://www.cdc.gov/h1n1flu/guidance/obstetric.htm.

Pregnant women who enter the hospital setting with illness from suspected or confirmed 2009 H1N1 influenza virus infection represent a special population warranting clinical management that considers the specific risks that 2009 H1N1 virus exposure poses to the newborn infant.

The location of the mother and newborn should be considered based on postpartum and/or newborn ward configuration and existing infection control policies. As clinically indicated, providers should consider a two-step process to manage postpartum and newborn care.

Step 1: Providers should consider temporarily separating the infected mother from the newborn within her room (in an isolette) or in separate rooms until the risk of infectious transmission is reduced, defined as having met ALL of the following criteria:

- The mother has received antiviral medications for at least 48 hours and;
- The mother is without fever for 24 hours without antipyretics and;
- The mother can control cough and respiratory secretions.

Once these criteria are met, the mother and infant can initiate close contact throughout the postpartum period with droplet precautions and the mother can begin infant feedings.

Step 2: Once the mother and infant are able to initiate close contact, the following guidance is offered for mothers immediately prior to feeding and handling the infant in order to protect the newborn from droplet exposure:

- The mother should wash her hands with soap and water;
- The mother should put on a face mask;
- The mother should observe all respiratory hygiene/ cough etiquette guidelines.

These precautions should be followed for 7 days after symptom onset or 24 hours after resolution of symptoms, whichever is longer.

Healthy term newborns of infected mothers with suspected or confirmed 2009 H1N1 should be considered exposed, rather than infected, if they are born in the hospital

setting following infection control guidelines. These infants should be observed for signs of infection. Unless clinically indicated, these newborns should be cared for with standard precautions whether they are cared for in the mother's room or in the term newborn nursery setting.

Pneumococcal Vaccination Recommendations

On November 16, CDC issued a Health Advisory encouraging the use of pneumococcal vaccines to help prevent secondary pneumococcal infections following infection with influenza viruses, including 2009 H1N1 virus, in at-risk persons. The following is from the CDC Health Advisory.

2009 H1N1 Pandemic Update: Pneumococcal Vaccination Recommended to Help Prevent Secondary Infections

Summary of Recommendations: *CDC's Advisory Committee on Immunization Practices (ACIP) recommends a single dose of pneumococcal polysaccharide vaccine (PPSV) for all people 65 years of age and older and for persons 2 through 64 years of age with certain high-risk conditions. Among those with high-risk conditions for pneumococcal disease, most are also at high risk for severe complications from influenza.* ***Special emphasis should be placed on vaccinating adults under 65 years of age who have established high-risk conditions for pneumococcal disease; PPSV coverage among this group is low and this group may be more likely to develop secondary bacterial pneumonia after an influenza infection.*** *All children younger than 5 years of age should continue to receive pneumococcal conjugate vaccine (PCV7) according to existing recommendations.*

Situation:
Streptococcus pneumoniae (pneumococcus) remains a leading cause of vaccine-preventable illness and death in the United States. Some of CDC's Active Bacterial Core surveillance (ABCs) sites have seen greater than expected numbers of cases of invasive pneumococcal disease coincident with increases in influenza-associated hospitalizations. A causal relationship between 2009 H1N1 influenza and this increase has not yet been established, but CDC is pursuing that question with state and local public health officials.

Influenza predisposes individuals to developing bacterial community-acquired pneumonia. During each of the influenza pandemics of the 20th century, secondary bacterial pneumonia was a frequent cause of illness and death and *S. pneumoniae* was reported as the most common etiology. These findings also apply to seasonal influenza. Recently, pneumococcal infections have been identified as an important complication in severe and fatal cases of 2009 H1N1 influenza virus infection. **A key difference between this pandemic and those of the past is that now we have two pneumococcal vaccines that may help to prevent these infections.**

Recommendations:
During the 2009-2010 influenza season, pneumococcal vaccines can be useful in preventing secondary pneumococcal infections and reducing illness and death among those infected with influenza viruses.

CDC's Advisory Committee on Immunization Practices (ACIP) recommends a single dose of pneumococcal polysaccharide vaccine (PPSV) for all people 65 years of age and older and for persons 2 through 64 years of age with certain high-risk conditions. For those 19 through 64 years of age, these include: having asthma or smoking cigarettes. For those 2 through 64 years of age, high-risk conditions include: chronic cardiovascular disease (congestive heart failure and cardiomyopathies), chronic pulmonary disease (including chronic obstructive pulmonary disease and emphysema), diabetes mellitus, alcoholism, chronic liver disease (including cirrhosis), cerebrospinal fluid leaks, cochlear implant, functional or anatomic asplenia including sickle cell disease and splenectomy, immunocompromising conditions including HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and those who have received an organ or bone marrow transplant, and residents of nursing homes or long-term care facilities.
Among those with high-risk conditions for pneumococcal disease, most are also at high risk for severe complications from influenza. A single pneumococcal revaccination at least five years after initial

vaccination is recommended for people 65 years and older who were first vaccinated before age 65 years. A single pneumococcal revaccination also is recommended for people at highest risk of disease, such as those who have functional and anatomical asplenia, and those who have HIV infection, AIDS or malignancy and have at least five years elapsed from receipt of first vaccination.

All people who have existing indications for PPSV should continue to be vaccinated according to current ACIP recommendations during the 2009 H1N1 influenza pandemic. **Special emphasis should be placed on vaccinating adults under 65 years of age who have established high-risk conditions for pneumococcal disease; PPSV coverage among this group is low and this group may be more likely to develop secondary bacterial pneumonia after an influenza infection.** PPSV is available for ordering through the usual process; ordering PPSV is not linked to placing orders for monovalent 2009 H1N1 influenza vaccine.

Use of PPSV among people without current indications for vaccination is not recommended at this time.

All children younger than 5 years of age should continue to receive pneumococcal conjugate vaccine (PCV7) according to existing recommendations.

According to existing guidelines, the use of a commercially available urine antigen test (Binax NOW®) is recommended for the diagnosis of pneumococcal pneumonia in adults. Such testing, along with blood cultures and testing for influenza infection, can assist clinicians in determining whether secondary pneumococcal pneumonia is occurring.

CDC recommends a yearly seasonal influenza vaccine as the first and most important step in protecting against seasonal influenza. Annual influenza vaccination is especially important for people at high risk of serious influenza complications, including young children, pregnant women, older adults, and people with certain chronic health conditions such as asthma, diabetes, heart or lung disease, and neurologic conditions [including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury]. Seasonal influenza vaccine also is important for health care workers and other people who live with or care for high risk people to prevent giving the influenza to those at high risk.

A new monovalent vaccine against 2009 H1N1 influenza is available and is our best option for prevention of 2009 H1N1 infection. People at greatest risk for 2009 H1N1 infection or serious complications and recommended to receive the first available doses of vaccine include children, young adults age 19-24, pregnant women, and people age 25-64 with chronic health conditions. Monovalent 2009 H1N1 influenza vaccine is important for close contacts of infants younger than 6 months of age and health care and emergency medical services personnel. While vaccine supply is currently less than demand, additional doses are becoming available daily and supply will increase through November and December.

In communities where 2009 H1N1 is circulating, treatment with influenza antiviral agents is recommended for all hospitalized patients with confirmed, probable or suspected 2009 H1N1 or seasonal influenza and for outpatients who are at higher risk for influenza-related complications. Empiric treatment of patients hospitalized with community acquired pneumonia should include both influenza antiviral agents and appropriate antibiotic therapy. For more information on treatment of influenza, see http://www.cdc.gov/h1n1flu/recommendations.htm.

For More Information:

- For Clinicians: Prevention Of Pneumococcal Infections Secondary To Seasonal And 2009 H1N1 Influenza Viruses Infection (http://www.cdc.gov/h1n1flu/vaccination/provider/provider_pneumococcal.htm)
- Pneumococcal Vaccine Website (http://www.cdc.gov/vaccines/vpd-vac/pneumo/default.htm)

- Interim guidance for use of 23-valent pneumococcal polysaccharide vaccine during novel influenza A (H1N1) outbreak (http://www.cdc.gov/h1n1flu/guidance/ppsv_h1n1.htm)
- CDC's Morbidity and Mortality Weekly Report (MMWR): Bacterial Coinfections in Lung Tissue Specimens from Fatal Cases of 2009 Pandemic Influenza A (H1N1) --- United States, May--August 2009; September 29, 2009 / 58(Early Release);1-4 (http://www.cdc.gov/mmwr/PDF/wk/mm5838.pdf)
- Table: ACIP Recommendations for Use of Pneumococcal Polysaccharide Vaccine (http://www.cdc.gov/h1n1flu/vaccination/provider/provider_pneumococcal.htm#table1)
- Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on Management of Community-Acquired Pneumonia in Adults (http://www.journals.uchicago.edu/doi/pdf/10.1086/511159)
- Preventing Seasonal Flu With Vaccination (http://www.cdc.gov/flu/protect/vaccine/index.htm)
- General Information About 2009 H1N1 Vaccines (http://www.cdc.gov/h1n1flu/vaccination/general.htm)
- Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season (http://www.cdc.gov/h1n1flu/recommendations.htm)
- Interim Recommendations for Clinical Use of Influenza Diagnostic Tests During the 2009-10 Influenza Season (http://www.cdc.gov/h1n1flu/guidance/diagnostic_tests.htm)
- Active Bacterial Core surveillance (http://www.cdc.gov/abcs)

In addition to the Health Advisory, the Director of CDC's National Center for Immunization and Respiratory Diseases has issued a letter to medical providers promoting the use of PPSV in adults. The letter points out that approximately 70 million persons with existing PPSV indications are unvaccinated, and providers are urged to ensure that all patients with indications receive the vaccine. Special emphasis should be placed on vaccinating adults under 65 years of age who have established high-risk conditions; PPSV coverage among this group is very low and this group may be more likely to develop secondary bacterial pneumonia after an influenza infection. The full text of the letter is available at http://www.cdc.gov/h1n1flu/vaccination/provider/lettertoprovider.htm.

CDC has also developed a set of general questions and answers on 2009 H1N1 influenza and pneumococcal disease. These are found at http://www.cdc.gov/h1n1flu/vaccination/qa_pneumococcal_disease.htm.

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html. Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).

Health Update:

2009 H1N1 Influenza Update 16: Recall of Certain Lots of H1N1 Pediatric Vaccine in Pre-Filled Syringes, Updated Recommendations for the Use of Antiviral Medications

December 15, 2009

This document will be updated as new information becomes available. The current version can always be viewed at http://www.dhss.mo.gov.

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Health Update
December 15, 2009

FROM: MARGARET T. DONNELLY
DIRECTOR

SUBJECT: 2009 H1N1 Influenza Update 16: Recall of Certain Lots of H1N1 Pediatric Vaccine in Pre-Filled Syringes, Updated Recommendations for the Use of Antiviral Medications

This Health Update provides information on: 1) the recall of certain lots of H1N1 pediatric vaccine, and 2) updated recommendations for the use of antiviral medications.

Recall of Certain Lots of H1N1 Pediatric Vaccine in Pre-Filled Syringes

The following is taken from a Health Update issued December 15 by the Centers for Disease Control and Prevention (CDC).

Non-Safety Related Voluntary Recall of Certain Lots of Sanofi Pasteur H1N1 Pediatric (0.25 mL, for 6-35 month olds) Vaccine in Pre-Filled Syringes

Summary: As part of its quality assurance program, Sanofi Pasteur, Inc., performs additional routine, ongoing testing of influenza vaccines after the vaccine has been distributed to health care providers to ensure that vaccines continue to meet required specifications. In recent testing of the amount of antigen in its influenza A (H1N1) monovalent vaccine, Sanofi Pasteur found four distributed lots of single-dose, pre-filled syringe pediatric (0.25 mL.) vaccine with antigen content lower than required potency levels. The manufacturer is conducting a non-safety related voluntary recall of these affected lots of vaccine.

Background

After performing these tests, Sanofi Pasteur notified the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) that the antigen content in one lot of pediatric syringes that had been distributed to providers was later found to have dropped below a pre-specified limit. As a result of this finding, Sanofi Pasteur tested additional lots and found that three other lots that had been distributed also had an antigen content that had fallen below pre-specified limits. This means that doses from these four vaccine lots no longer meet the specifications for antigen content.

Recommendations

While the antigen content of these lots is now below the specification limit for the product, CDC and FDA are in agreement that the small decrease in antigen content is unlikely to result in a clinically significant reduction in immune response among persons who have received the vaccine. For this reason, there is no need to revaccinate persons who have received vaccine from these lots.

Providers are being asked to return any vaccine to the manufacturer in the following lots that remains unused to the manufacturer:

- 0.25 mL pre-filled syringes, 10-packs (NDC # 49281-650-25, sometimes coded as 49281-0650-25):
  UT023DA
  UT028DA
  UT028CB

- 0.25 mL pre-filled syringes, 25-packs (NDC # 49281-650-70, sometimes coded as 49281-0650-70):
  UT030CA

These lots were shipped in November and are intended for children 6 months through 35 months of age. Sanofi Pasteur will send directions for returning unused vaccine from these lots to providers.

All vaccines are thoroughly tested prior to release and shipping to determine that they meet all manufacturer and FDA standards for purity, potency and safety. The affected vaccine met all specifications at the time of release. CDC and FDA have determined that there are no safety concerns for children who have received this vaccine. Sanofi Pasteur has discontinued distribution of the 0.25 mL syringes of H1N1 pediatric vaccines.

The drop in antigen content below the required specification that is described here is specific to Sanofi Pasteur's pediatric H1N1 monovalent vaccine in 0.25 mL pre-filled syringes. The same vaccine packaged in other forms, such as 0.5 mL pre-filled syringes for older children and adults and multi-dose vials, continue to meet specifications.

The antigen content in the affected lots of vaccine is only slightly below the specification limit. The slightly reduced concentration of vaccine antigen found in retesting these lots is still expected to be effective in stimulating a protective response. There is no need to re-administer a dose to those who received vaccine from these lots. However, as is recommended for all 2009 H1N1 vaccines, all children less than 10 years old should get the recommended two doses of H1N1 vaccine approximately a month apart for the optimal immune response. So, children less than 10 years old who have only received one dose of vaccine thus far should still receive a second dose of 2009 H1N1 vaccine.

For children 6 months of age and older, vaccine is available in multidose vials. The vaccine in multidose vials is safe and effective vaccine for children. One difference between vaccine in pre-filled syringes and the multidose vials is that the multidose vials contain a preservative (thimerosal) to prevent potential contamination after the vial is opened. The standard dose for this preparation for administration to infants 6-35 months old is the same as for the pre-filled syringes, 0.25 mL. For healthy children at least 2 years of age, the nasal spray (live, attenuated influenza vaccine) is also an option. The nasal spray vaccine is produced in single units that do not contain thimerosal.

For More Information:

- For Questions and Answers related to the withdrawn vaccine see http://www.cdc.gov/h1n1flu/vaccination/syringes_qa.htm
- Call CDC's toll-free information line, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, which is available 24 hours a day, every day.

Updated Recommendations for the Use of Antiviral Medications in Treatment and Prevention of Influenza

On December 7, CDC updated its recommendations for the use of antiviral drugs for treatment and prevention of influenza. *Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season* is available at http://www.cdc.gov/h1n1flu/recommendations.htm. Specific updates include the following:

1. Information regarding use of intravenous peramivir under an Emergency Use Authorization.
2. Information on availability of renal dosing for peramivir.
3. Updated oseltamivir dosing instructions for children younger than 1 year of age based on weight.
4. Antiviral treatment and chemoprophylaxis considerations for patients vaccinated with 2009 H1N1 and seasonal influenza vaccines.

5. Guidance on early empiric antiviral treatment for patients with progressive or severe influenza-like illness, regardless of underlying medical conditions.
6. Guidance on early empiric antiviral treatment for patients with underlying medical conditions placing them at risk for complications.
7. Clarification of treatment considerations for patients with illness longer than 48 hours.

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html. Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).

Health Update:

2009 H1N1 Influenza Update 17: Non-Safety-Related Recall of Specific Lots of H1N1 Influenza Nasal Spray Vaccine

December 23, 2009

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Health Update
December 23, 2009

FROM: MARGARET T. DONNELLY
DIRECTOR

SUBJECT: 2009 H1N1 Influenza Update 17: Non-Safety-Related Recall of Specific Lots of H1N1 Influenza Nasal Spray Vaccine

On December 23, 2009, the Centers for Disease Control and Prevention (CDC) issued the following Health Update.

MedImmune Monovalent 2009 (H1N1) Influenza Nasal Spray Vaccine — Shortened Shelf Life of Certain Lots

MedImmune announces limited, voluntary, non-safety-related recall of remaining unused product

Summary
On December 18 and 21, MedImmune notified CDC and FDA that the potency of 13 lots of monovalent 2009 (H1N1) nasal spray vaccine had decreased below a pre-specified limit or were at risk of falling below that limit in the next week. This slight decrease in vaccine potency is not expected to have an impact on the protective response to vaccination. There are no safety concerns with these lots of 2009 H1N1 vaccine. All lots successfully passed pre-release testing for purity, potency and safety. However, because their potency is now or might soon be below the specified lower limit, MedImmune will send providers directions for returning any unused vaccine from these lots.

Recommendations
The potency of these lots is now or might soon be slightly below the specified range for the product. CDC and FDA are in agreement that the slight decrease in vaccine potency is not expected to have an impact on the protective response to vaccination. For this reason, there is no need to revaccinate persons who have received vaccine from these lots.

People who received vaccine from the recalled lots do not need to take any action. Children and adults aged 10 years and older who received the vaccine do not need any further doses of vaccine. As is recommended for all 2009 H1N1 vaccines, all children younger than 10 years old should get the recommended two doses of 2009 H1N1 vaccine approximately a month apart. Therefore, children younger than 10 years old who have only received one dose of vaccine thus far should still receive a second dose of 2009 H1N1 vaccine. It is best to use the same type of vaccine for the first and second doses.

Background
As part of its quality assurance program, the manufacturer of the nasal spray 2009 H1N1 influenza vaccine, MedImmune, performs routine, ongoing stability testing of the vaccine after it has been shipped to providers. Stability testing means measuring the strength of a vaccine over time.

The 13 lots subject to the recall include approximately 4.7 million doses. These doses were shipped to CDC's contract distributor in October and early November. **Most of the doses are believed to have already been administered while fully potent and within specifications.** However, there are almost certainly some doses that have not yet been used.

The potency issue described here is specific to the 13 lots of nasal spray 2009 H1N1 influenza vaccine listed below. Subsequent lots of the vaccine were produced with a slightly higher initial potency to decrease the chance that the potency would fall "below specification" before their expiration dates. Following its routine practice, the manufacturer will continue to monitor the stability of these subsequent lots.

This recall does not affect 2009 H1N1 vaccine produced by other manufacturers. However, a similar recall was conducted recently, which involved lots from Sanofi Pasteur's pediatric 2009 H1N1 vaccine in 0.25 mL pre-filled syringes. (See http://www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00303)

Before they were shipped, the lots currently being recalled passed all quality controls and met all specifications for safety, purity, and potency.

MedImmune will send a notification to providers who received doses from any of the 13 lots of vaccine so that they can return any unused vaccine.

Lot Information
Providers are being asked to return any vaccine in the following lots that remains unused to the manufacturer:

- 500754P
- 500751P
- 500756P
- 500757P
- 500758P
- 500759P
- 500760P
- 500761P
- 500762P
- 500763P
- 500764P
- 500765P
- 500776P

For More Information:
For information about the recalled vaccine, see
http://www.cdc.gov/h1n1flu/vaccination/sprayrecall_qa.htm.

Call CDC's toll-free information line, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, available 24/7.

For manufacturer's information about the recall, see
http://www.medimmune.com/pdf/H1N1_Recall_QandA_122209.pdf

For manufacturer's instructions to providers on actions to be taken, see
http://www.medimmune.com/pdf/H1N1_Recall_letter_122209.pdf

Links to comprehensive information and guidance for medical professionals on 2009 H1N1 influenza are available at http://www.dhss.mo.gov/BT_Response/_MedProfs.html. Links to comprehensive information and guidance on seasonal influenza are found at http://www.dhss.mo.gov/PandemicInfluenza/MedSeasonalFlu.html.

Missourians, including Missouri medical professionals, now have access to a toll-free H1N1 influenza information line. Named the **H1N1 InfoLine**, and sponsored by DHSS, it can provide information and guidance on 2009 H1N1 influenza and H1N1 vaccine to both the public and medical providers. This service is available 24 hours a day, seven days a week at 1-877-FLU-4141 (1-877-358-4141).